Comparison of clinical outcome and patency of Gore-Viatorr and Niti-S stents used in Transjugular intrahepatic portosystemic shunt (TIPS)

A dissertation submitted in partial fulfillment of MD Radiodiagnosis (Branch VIII) examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2018

DECLARATION

I declare that the dissertation entitled **"**Comparison of clinical outcome and patency of Gore-Viatorr and Niti-S stents used in Transjugular intrahepatic portosystemic shunt (TIPS)**"** is my original work done in partial fulfillment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2018

Dr. Manisha Sheshrao Mane
Post graduate student (MD Radiodiagnosis)
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CERTIFICATE

I declare that the dissertation entitled **"**Comparison of clinical outcome and patency of Gore-Viatorr and Niti-S stents used in Transjugular intrahepatic portosystemic shunt (TIPS)**"** is my original work done in partial fulfillment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2018.

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Associate Proffesor,
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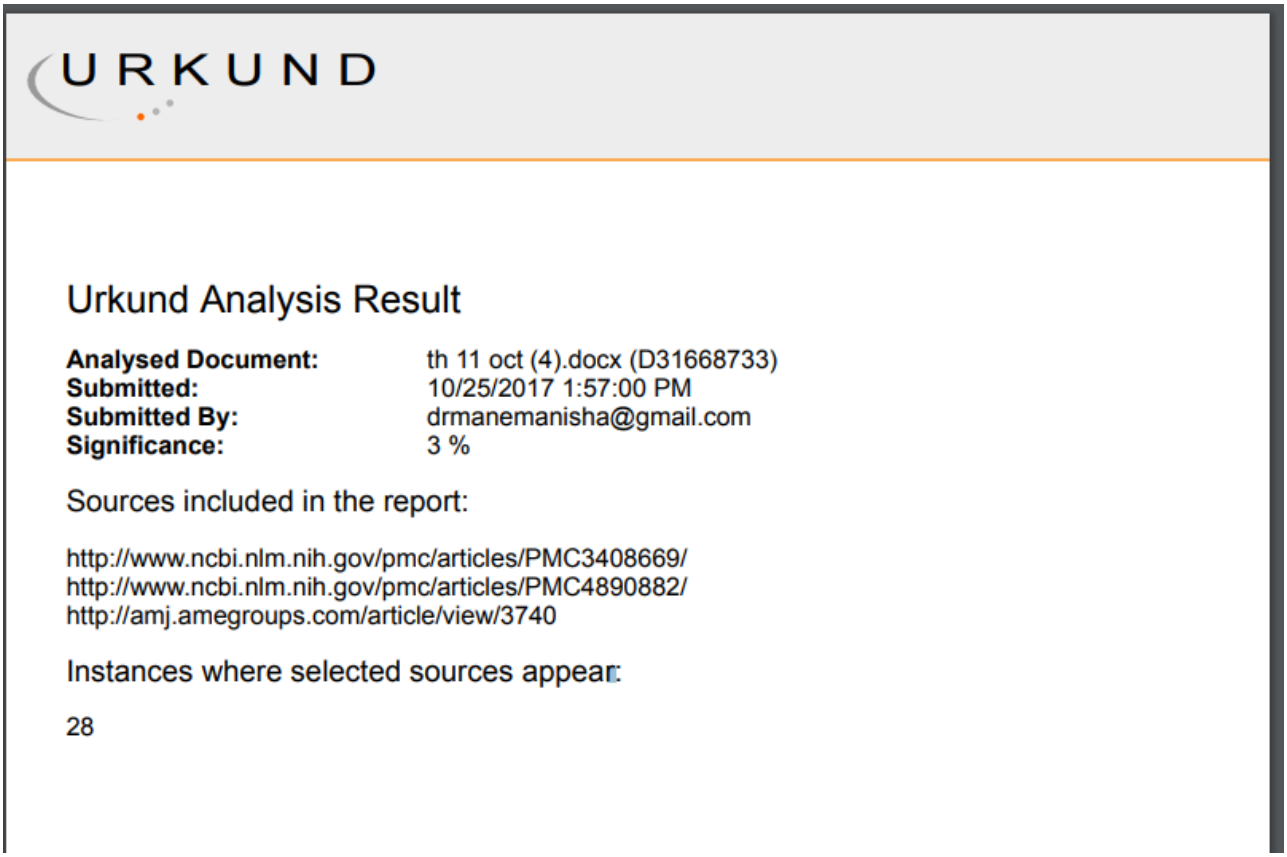
PLAGIARISM CERTIFICATE



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September 20, 2016

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Comparison of clinical outcome and patency of different types of stents used in Transjugular intrahepatic portosystemic shunt (TIPS)
Dr. Manisha Sheshrao Mane (Employment Number: 33298), Radiology, Dr. Munawwar Ahmed (Employment Number: 32015), Dr. Shyamkumar N. Keshava, Radiology, Dr. Vinu Moses (Employment number: 28371), Radiology, Dr. George Koshy Chiramel, Radiology, Dr. C.E.Eapen, Clinical Gastroenterology and Hepatology, Dr. Uday George Zachariah, Hepatology.. Dr. Ashish Goel, Hepatology.

Ref: IRB Min No: 9963 [OBSERVE] dated 02.03.2016

Dear Dr. Manisha Sheshrao Mane,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
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Cc: Dr. Munawwar Ahmed, Radiology, CMC, Vellore

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Ref: IRB Min No: 9963 [OBSERVE] dated 02.03.2016

Dear Dr. Manisha Sheshrao Mane,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Comparison of clinical outcome and patency of different types of stents used in Transjugular intrahepatic portosystemic shunt (TIPS)" on March 02nd 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Proforma
3. Patient Information Sheet and Informed Consent Form (English, Tamil, Bengali, Hindi)
4. Cvs of Drs. Ashish Goel, Eapen, Munawwar Ahmed, Shyam Kumar, Uday Zachariah, Vinu Moses, George Koshy, Manisha.
5. No. of documents 1 - 4

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on March 02nd 2016 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
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Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho
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Secretary, Ethics Committee, IRB
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Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, Vellore	External, Scientist &Epidemiologist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Visalakshi. J	MPH, PhD	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
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Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. B. J. Prashantham	MA(Counseling Psychol MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centr Vellore	External, Social Scientist
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Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
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Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Comparison of clinical outcome and patency of different types of stents used in Transjugular intrahepatic portosystemic shunt (TIPS)" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of Rs. 98,800/-(Ninety Eight Thousand Eight hundred only) for 14 months.

Yours sincerely

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.,
SECRETARY - (ETHICS COMMITTEE)
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Christian Medical College, Vellore - 632 002.

IRB Min No: 9963 [OBSERVE] dated 02.03.2016

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I wish to specially thank all radiographers and nursing staff posted in DSA Room 22 .
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CMC Vellore and all my teachers, for making this study and this course a reality.
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My family, friends and colleagues for their love, constant support and encouragement.
And to the Lord Almighty for all his blessings, throughout my life

Table of Contents

INTRODUCTION:

TIPS (Transjugular intrahepatic portosystemic shunt) is an image guided intrahepatic parenchymal shunt created between portal vein and systemic circulation [hepatic vein or inferior vena cava] (1).

Creation of this shunt helps in diverting blood flow away from portal system and reduces the portal pressure. Reduction of the portal pressure decreases the risk of variceal bleeding, recurrent ascites and hydrothorax. Thus TIPS is a useful modality for treating complications of portal hypertension like refractory ascites, acute or recurrent variceal haemorrhage, hepatic hydrothorax, hepato-renal syndrome and hepatopulmonary syndrome. It is also useful for treating Budd Chiari and act as bridge to liver transplant (1).

If the intrahepatic shunt is created between portal vein and hepatic vein the procedure is called TIPS (Transjugular intrahepatic portosystemic shunt) as shown in figure 1a.(1). If instead of hepatic vein inferior vena cava is punctured directly the procedure is called as Direct intrahepatic portosystemic shunt as shown in figure 1b.

Figure 1a: Schematic representation of TIPS

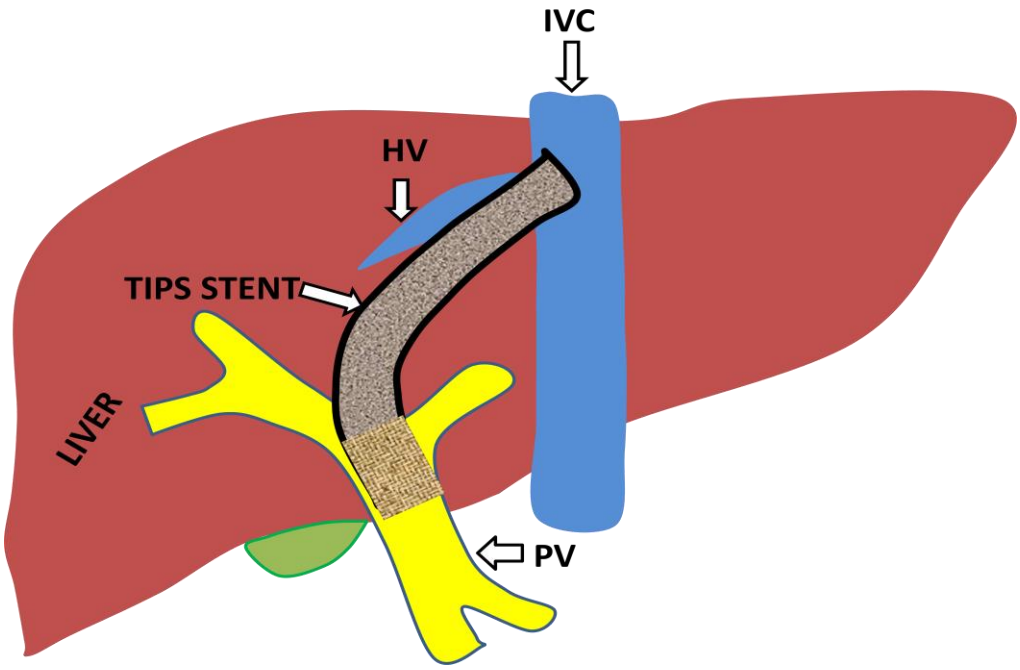
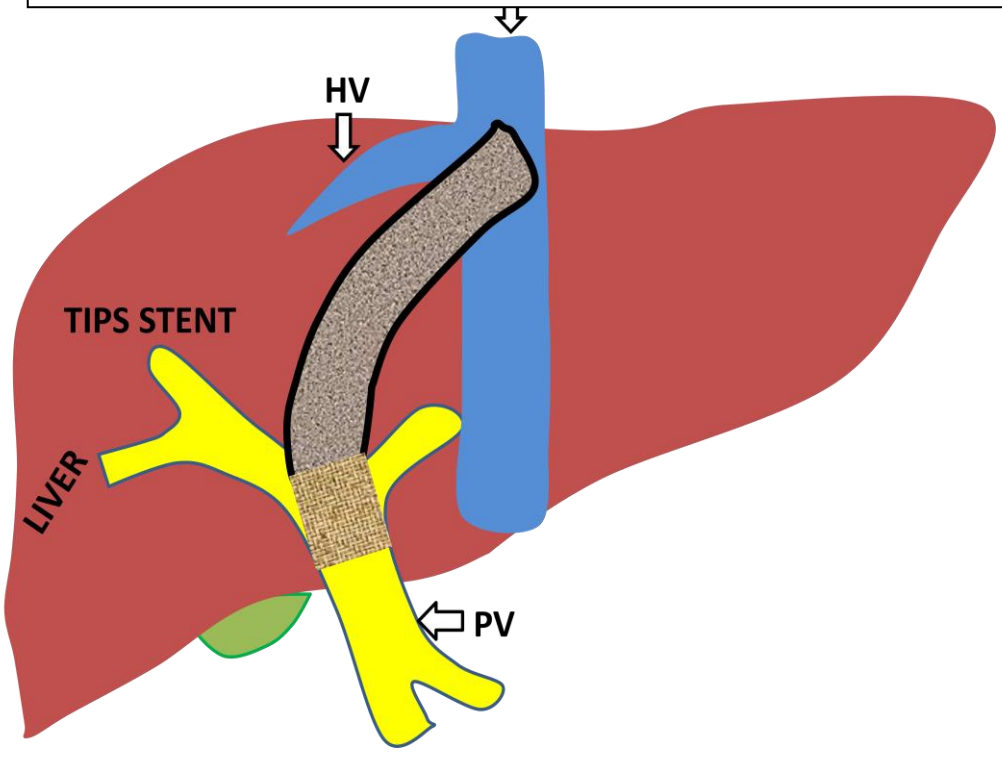


FIGURE 1b: Schematic representation of Direct TIPS



In the early years bare metal stents were used, higher shunt failure rate was the major drawback of these stents. With the introduction of covered stents especially Gore Viatorr, shunt patency significantly improved. Which in turn improved the symptom free survival time and decreased the morbidity (2).

AIM:

Comparison of clinical outcome and patency of Gore-Viatorr and Niti-S stents used in Transjugular intrahepatic portosystemic shunt (TIPS).

OBJECTIVES:

1) To compare primary patency at 3 months and secondary patency rates at 24 months of Gore-Viatorr and Niti-S stents

2) Which stent has the best primary patency rate?

3) Compare clinical outcome of Gore-Viatorr and Niti-S stents

REVIEW OF LITERATURE:

History and evolution:

TIPS(Transjugular intrahepatic portosystemic shunt) was first introduced by Rosch et al in 1969 (3).

In 1982, Colaptino performed this procedure in a cirrhotic patient using a balloon catheter for the first time (4).

Early occlusion of the shunt within a short period due to unsupported parenchymal shunt was a problem initially. Patency of the shunt improved with the placement of the stent in the shunt.

In 1988 in Freiburg, first TIPS was performed by using metallic Palmaz stent (5).

With the introduction of USG guidance for visualisation of the portal vein there was significant reduction in the time taken for the procedure and complications (5).

In 1990 about 50 patients and from 1990 to 1995 about 500 patients were treated using the same technique (5).

In the past 29 years due to better definition of indications, better patient selection and improvement in the techniques have resulted in improved clinical outcome (1).

Current status:

Currently TIPS is a well established procedure usually done by interventional radiologist. It is used worldwide for treating and managing complications related to portal hypertension (7). It is usually performed as an elective procedure, however in the setting of acute variceal bleed it is also performed on an emergency basis within 24 hours of acute variceal bleed not controlled by 2 endoscopic therapies (8).

In the early years due to use of bare metal stents, incidence of shunt dysfunction and shunt occlusion was much higher which resulted in higher frequency of shunt revisions. Once the PTFE covered stent was introduced shunt patency rate significantly improved by reducing the number of shunt revisions. This also improved the clinical outcome of the patients by increasing the symptom free time period (6).

Amongst the various covered stents used Gore-Viatorr endoprosthesis is the most commonly used stent.

With technical improvement in the skills and stents there is increase in the shunt patency and reduction in the complications. In patients with Budd Chiari syndrome not responding to medical therapy TIPS is considered as treatment of choice. By offering increased symptom free period it has reduced the need for liver transplant (5).

INDICATIONS:

Portal hypertension is the main complication of cirrhosis of liver. In normal individuals pressure difference in portal vein and hepatic vein or right atrium is upto

5mm Hg. Portal pressure gradient more than 6mm is defined as portal hypertension. Whenever this gradient crosses 10-12mm Hg mark clinical signs start to develop (9). To reduce this portal pressure multiple collaterals develop as a compensatory mechanism and cause variceal bleeding. Raised portal pressure also results in development of ascites and hepatorenal syndrome (10).

Indications for TIPS procedure are listed below:

1) Variceal bleeding:

TIPS is most commonly performed for the treatment of refractory variceal bleeding. TIPS is useful both for controlling and preventing variceal bleed. In the setting of acute variceal bleeding, if the bleed is not controlled after 2 sets of endoscopic therapies within 24 hours TIPS can be placed. TIPS is also useful in case of refractory esophageal variceal bleeding unresponsive to medical treatment and endoscopic sclerotherapy or ligation. It is not recommended as first line treatment for variceal bleed but is reserved in cases of refractory variceal bleed (11).

Various meta-analysis published in the last decade suggested three times decrease in the rate of recurrent variceal bleeding after TIPS placement in comparision to endoscopic therapies (12).

2) Refractory ascites:

Refractory ascites is recurrence of ascites inspite of sodium restriction and diuretic therapy. If untreated patient can develop many complications like spontaneous

bacterial peritonitis, hepatorenal syndrome and hydrothorax. Large volume paracentesis (LVP) is a first line treatment for refractory ascites. Many studies have shown that TIPS is a better treatment option compared to LVP for control of refractory ascites.

Portal hypertension results due to obstruction to the splanchnic blood flow, this obstruction causes circulatory disturbances and increased portal, renal and splanchnic resistance. Placement of TIPS relieves the obstruction with redistribution of circulatory heamodyamics causing decrease in the renal resistance and in turn improving renal function.

Thus TIPS has an added advantage of improving the renal function in addition to control of ascites. Though LVP is a simpler procedure to perform and gives immediate relief cannot be used for long term management of refractory ascites due to its negative impact on renal function (5).

Various randomised controlled studies have shown inconsistent results in terms of survival. Some of the studies do not show any improvement in post TIPS survival rate, whereas some have shown better survival in patients with TIPS placement (5).

3) Hepatorenal syndrome:

As mentioned above TIPS improves the renal blood flow and in turn improves the renal function. Hence TIPS has a role in patients suffering from hepatorenal syndrome (5).

4) Hepatic hydrothorax:

Development of large pleural effusion in cirrhotics in absence of cardiac or pulmonary cause is termed as hepatic hydrothorax (12). Ascitic fluid tracks through diaphragmatic defects in to the pleural cavity (5).

When compared to other treatments, TIPS offers better control over the hepatic hydrothorax and also prolongs the survival (5).

5) Budd- Chiari syndrome:

Budd Chiari syndrome results due to obstruction of the hepatic vein or IVC occlusion. This results in portal hypertension. TIPS has a role in treatment of Budd Chiari when medical treatment fails and hepatic veins are damaged so that angioplasty and stenting of the vein is not possible. (13). As hepatic veins are damaged direct communication is created between IVC and portal vein which is called as DIPS (5). It was first performed in 2001(7).

Placement of TIPS relieves hepatic blood flow obstruction, improves arterial perfusion there by improving hepatocyte function (13)

6) Extrahepatic portal venous obstruction (EHPVO):

TIPS can be alternative option for management of variceal bleeding related to EHPVO. It is less invasive compared to surgery and is a valuable treatment in case of failure of surgery and endoscopic treatment(14).

Contraindications:

There are many contraindications for TIPS procedure.

Absolute and relative contraindications are listed in table (1) shown below (15)

Absolute contraindications	Relative contraindications
1. Heart failure 2. Severe pulmonary hypertension 3. Severe tricuspid regurgitation 4. Multiple liver cysts 5. Sepsis 6. Unresolved biliary obstruction	7. Central hepatoma 8. Severe coagulopathy 9. Thrombocytopenia (less than 20,000) 10. Moderate pulmonary hypertension 11.Hepatic artery or celiac artery stenosis

Complications:

Technical complications like capsule perforation, peritoneal haemorrhage and hemobilia were more frequent in the beginning. With the use of ultrasound guidance for puncture of the liver and portal vein these complications are almost not

encountered these days. Other complications like maldeployement, misplacement and migration of the stent are also very rare these days due to use of Gore-Viatorrstent (5).

Shunt dysfunction, hepatic encephalopathy and liver failure are the major complications of TIPS procedure (5).

1) Hepatic encephalopathy (HE):

TIPS placement results in diversion of blood flow to the systemic circulation and reduced liver perfusion (9). Increase delivery of nitrogen substances to brain increases the risk of hepatic encephalopathy (7).Worsening of pre-existing HE is also noted (10). Deranged liver function specifically raised bilirubin, advanced age and pre-existing HE are associated with increased risk of HE (5).

Using left branch of portal vein instead of right branch can reduce the risk of HE (16). Under dilating or reducing the size of the stents only up to 8mm rather than 10mm also reduces the risk of HE by reducing the shunt volume (5).

Patients developing hepatic encephalopathy are managed with medical treatment. Very few patients who develop severe HE and do not respond to medical treatment are indications for shunt diameter reduction or TIPS occlusion. Shunt reduction can be achieved by deploying hour glass stent within the previously placed stent (17).

2) Hepatic failure:

It is characterised by rapid derangement of liver function post TIPS placement. Reduction of liver perfusion post TIPS results in worsening of liver function (17). It carries poor prognosis and high mortality rate if not treated (5).

3) Endotipsitis:

It is a rare complication of TIPS and should be suspected in patients with persistent and unexplained bacteraemia. Treatment options include antibiotics for rest of life or liver transplant (17).

4) Hernia incarceration:

Placement of TIPS resolves massive ascites leading to alteration in the configuration of bowel and peritoneal anatomy. This leads to entrapment of bowel, ischemia and necrosis leading to need for surgery (17).

5) TIPS occlusion:

Early occlusion:

It is common with bare metal stents and occurs due to leakage of bile secondary to formation of biliary venous fistula. Bile is thrombogenic which predisposes to thrombus formation and results is acute occlusion of the stent. Hypercoagulable state is a predisposing factor for early occlusion of the stent and patients with repeated occlusions should undergo investigations to rule out the same (17). Occlusion results in recurrence of symptoms, bowel ischemia can occur due to extension of thrombus in mesenteric veins warranting treatment (18). Acute occlusion is treated with mechanical thrombectomy or catheter guided instent local thrombolysis followed by angioplasty (17). Urokinase and heparin are effective for local thrombolysis (19).

With the wide spread use of Gore-Viatorr endo-prosthesis acute occlusion of the stent is uncommon. As this prosthesis is covered it prevents the biliary-venous fistula formation and instent biliary leakage (17).

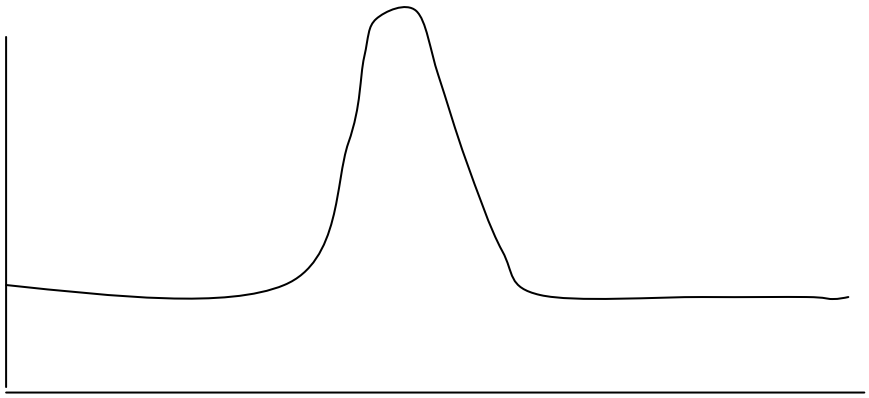
Gore-Viatorr prosthesis more commonly gets thrombosed due to obstruction to the blood flow secondary to the structural causes. Structural obstruction occurs following suboptimal positioning of the stent or migration of the stent (16).

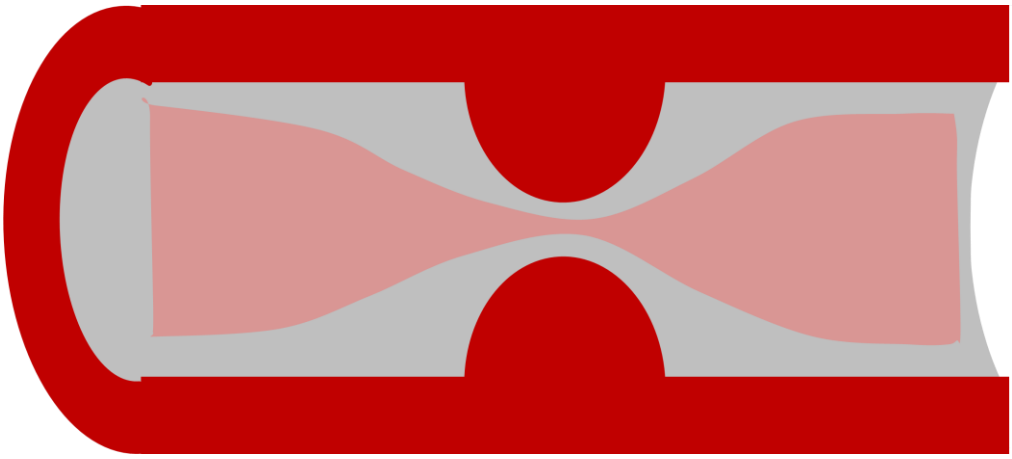
While performing the TIPS procedure during removal of guidewire/catheter can cause alteration of the stent configuration resulting obstruction to the flow.

Pseudointimal hyperplasia is another reason for shunt dysfunction which causes shunt stenosis (18).Pseudoitimal hyperplasia results due to aggregation of platelets, inflammatory cells, RBCs, myofibroblasts and fibrin which form a layer of granulation tissue. Prior thrombosis and biliary leakage both act as triggering factor for overgrowth of pseudointima (20).

Pseudointimal hyperplasia can cause simple or complex stent stenosis. Simple stenosis results due to focal narrowing of the stent secondary to intimal proliferation leading to web formation. Area of focal narrowing shows increased velocity hence is easy to detect simple stenosis on USG and Doppler examination.

Figure 2a: **Simple stenosis: velocities reliable**

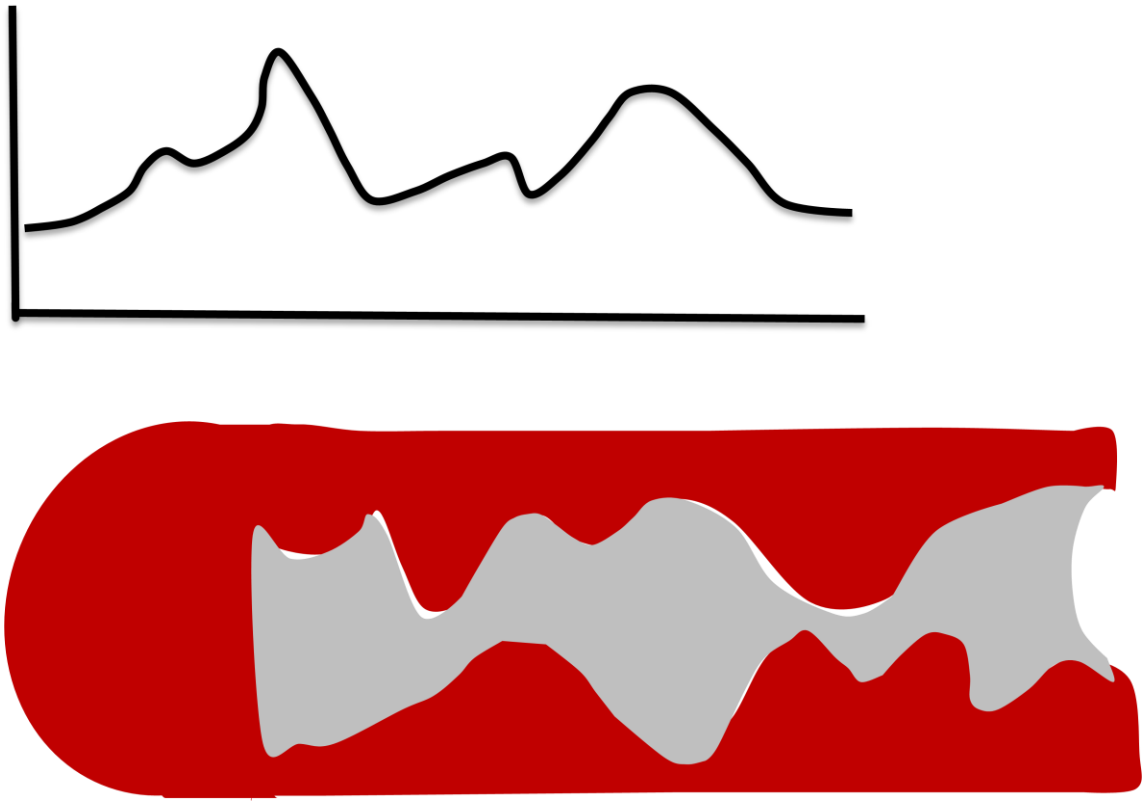




Complex stenosis results due to variable thickness of the pseudointima lining the stent. In this case Doppler of the stent is not reliable and needs evaluation of portal vein velocity. Reduction of portal vein velocity ranging between 10-20cm/sec suggests stent dysfunction in this setting (5).

As intimal hyperplasia results due to continuing platelet aggregation, platelet aggregation inhibitors and platelet derived growth factor inhibitors can be useful (19).

Figure 2b: Complex stenosis: velocities are unreliable



6) Radiation dose related complications:

TIPS procedure can be prolonged resulting in increased radiation dose exposure to the patient as well as the intervention radiologist. Deterministic effects like skin erthema, ulceration can result (21).

Various types of stents:

In the beginning bare metal stents were used which included Palmaz stent, Wall stent and Strecker stents. Examples of covered stents are Gore-Viatorr, (W.L. **Gore**, Flagstaff, AZ)., Fluency covered stent [Bard] and Niti-S stent (Niti-S stent; Taewoong, Seoul, Korea) (22). Multiple studies have been performed to analyze various materials used for covering the stent. Amongst them polytetrafluoroethylene (PTFE) has given best results (7). Long term shunt patency was significantly improved following introduction of covered stent (23).

Amongst the various covered stents used, Gore Viatorr stent is most commonly used stent.

Various stents used in Department of Radiology, CMC Vellore are

-Gore Viatorr stent

-Uncovered stent

-Covered-Uncovered stents combination

- Niti-S TIPS stent

Gore Viatorr stent:

It was introduced in 1999, after European multicenter trial, available since 2001, FDA approval in December 2004 (24).

In India it is available since 2005.

Structural support is provided by an external self-expanding nitinol stent (25).

Intrahepatic portion of the stent is covered with PTFE whereas the bare part lies in the portal vein (8).

Covered and uncovered portion, interface is demarcated by radio-opaque gold ring (25). This demarcation is useful for positioning of the stent during the procedure (26).

Additional radiopaque gold marker is at the proximal end which helps fluoroscopic visualisation during deployment (8).

Covered portion has 3 layers of PTFE with varying pore diameters which completely blocks the instent biliary leakage. It also prevents growth of liver tissue within the stent and covers part of the hepatic vein neat the puncture site. All these factors help in preventing thrombosis of stent (27).

Fluency stent:

It also is covered by PTFE but has 2 layers instead of 3 layers.

Covering is not same as VG, uses carbon along the inner layer which prevents platelet aggregation (23).

Angermayr et all have retrospectively demonstrated an improved survival rate of 88% at 1 year for patients treated with the VIATORR1endoprosthesis for TIPS, compared with 73% for a matched group receiving bare stents. Survival rate after TIPS creation with the VIATORR device is higher than that after TIPS creation with an uncovered stent (8).

Niti-S TIPS stent:

This stent has been used exclusively in our department since 2015 onwards as Gore Viatorr is not available in India.

Niti-S TIPS stent is being used since 2015 onwards as Gore Viatorr is not available in India. English literature available about Niti-S TIPS stent patency and clinical outcome are sparse and furthermore no Indian study is available.

It is a mesh-type stent interlaced with a nitinol monofilament (25).

Nitinol monofilament wire is wound on a mandrel to create a spiral mesh at deployment, the stent self-expands to a predetermined diameter of 8–10 mm with a length of 6–10 cm (20).

It has constant 20mm uncovered portion and variable covered portion [varying from 40mm to 100mm (20).

Technique of TIPS procedure:

It can be performed using sedation or under general anaesthesia. After puncturing the right internal jugular vein, IVC is accessed and catheter venogram is taken and pressures in the right atrium and IVC is measured. Right branch of portal vein is punctured and portogram is done, pressure in the portal vein is measured. Intrahepatic parenchymal track is dilated using balloon catheter. Stent is deployed within this intra-parenchymal track after which post TIPS pressures are measured.

Variations in the TIPS procedure technique:

Intravascular ultrasound can be used to guide the puncture while performing TIPS (25).

In the setting of jugular vein thrombosis femoral vein can be used for access (7).

In case of occluded portal vein, portal vein can be accessed through percutaneous approach which is combined with Transjugular approach. Percutaneous approach allows easy access to the portal vein which can be then recanalised. Balloon is inflated within this recanalised portal vein. Using the Transjugular approach needle is targeted to the inflated balloon in the portal vein. Once the balloon is punctured it assures that the needle is in the portal vein (7).

Monitoring TIPS patients:

Monitoring of TIPS patients need follow up at regular intervals, usually it is done at 1st week, at 3 months, at 6 months and yearly thereafter if no symptoms develop. If there is worsening of symptoms or development of new symptoms patient is advised to follow up immediately (28).

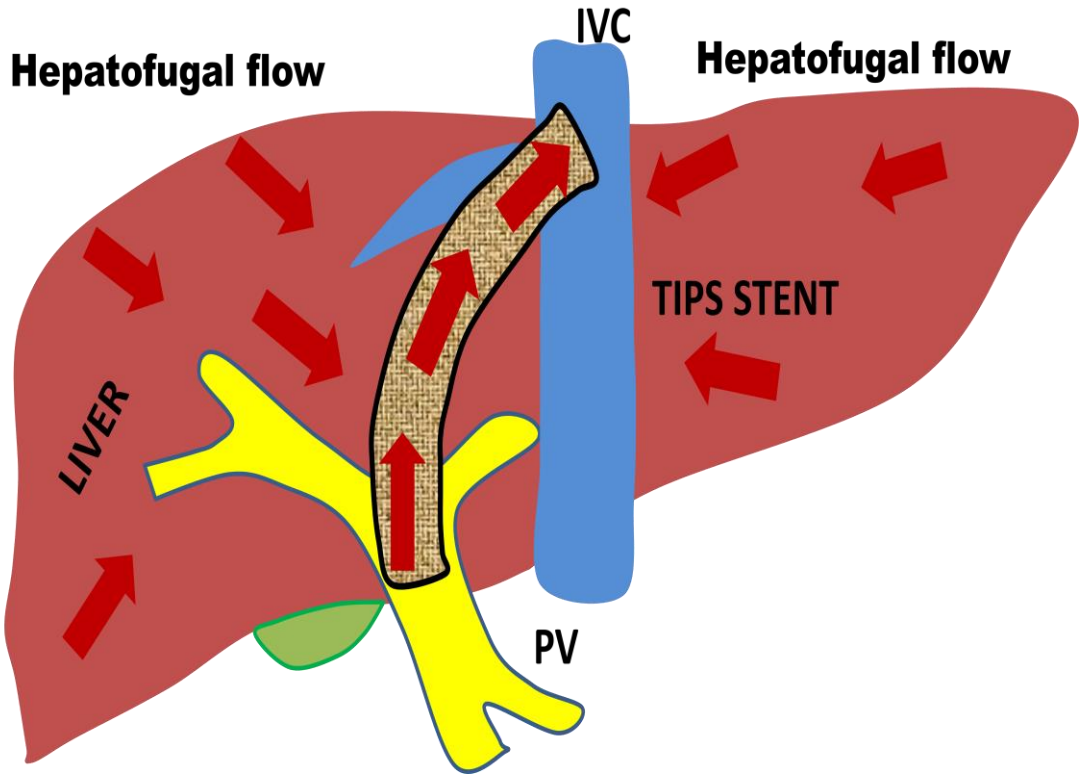
Regular follow up involves clinical assessment, Doppler evaluation and laboratory parameter evaluation. Clinical evaluation involves assessment of decrease in the symptoms, worsening of symptoms or development of new symptoms.

Doppler is an important investigation to check the shunt patency. Before interpreting the Doppler findings it is important to be aware of the normal anatomy and normal flow pattern of the shunt.

Shunt has 3 parts, caval end of shunt is called as cephalic part, portal end is called as caudal end with intervening segment is called as mid stent.

As this shunt is a low resistance pathway blood from the portal end flows towards the caval end, hence normal direction of flow within the stent is hepatofugal.

Figure 3a: normal flow pattern in shunt



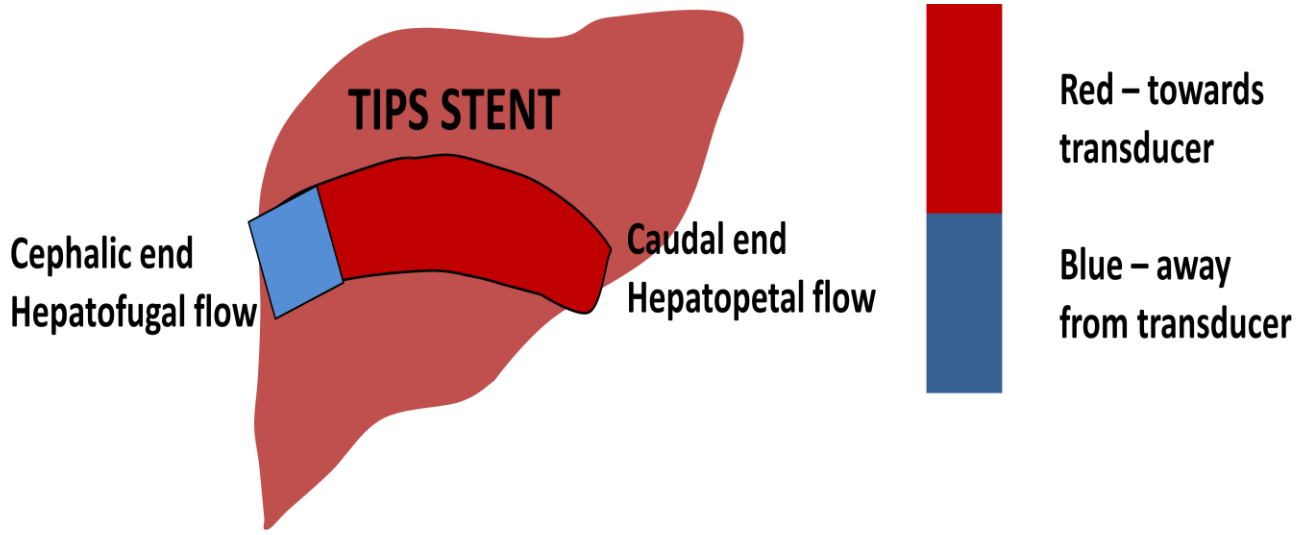


Figure 3b showing flow pattern in shunt

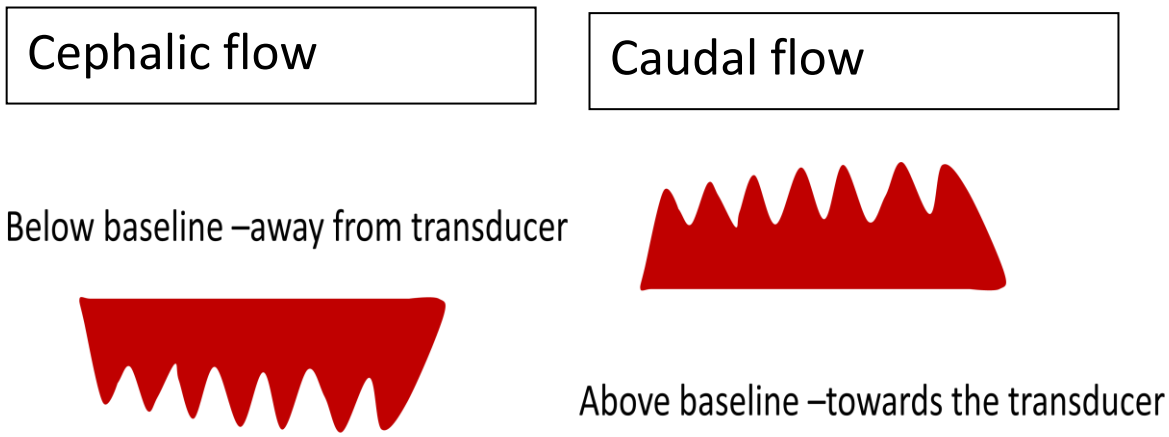


Figure 3c showing flow pattern in shunt

Shunt can show complete/ partial thrombosis or stenosis in a particular region. In case of complete thrombosis there will be complete absence of colour flow in the stent.

Stenosed segment will show high velocities within. Shunt velocities are usually taken at portal end, mid part of the stent and caval end of the stent. Velocities more than 180cm/sec and less than 90 cm/sec are considered abnormal or change in velocity by 50cm/sec is also considered abnormal. Main portal vein velocity more than 30 cm/sec is considered normal. Post TIPS patients show hepatofugal flow. Change in the hepatofugal flow to hepatopetal flow is considered abnormal. Presence of new or increased collateral vessel also suggests TIPS dysfunction (29).

Cirrhotic patients are also checked for development of any focal lesions in the liver if so these lesions need further evaluation to rule out hepatocellular carcinoma.

Along with this patients also undergo laboratory parameter evaluation which includes

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Role of other imaging modalities:

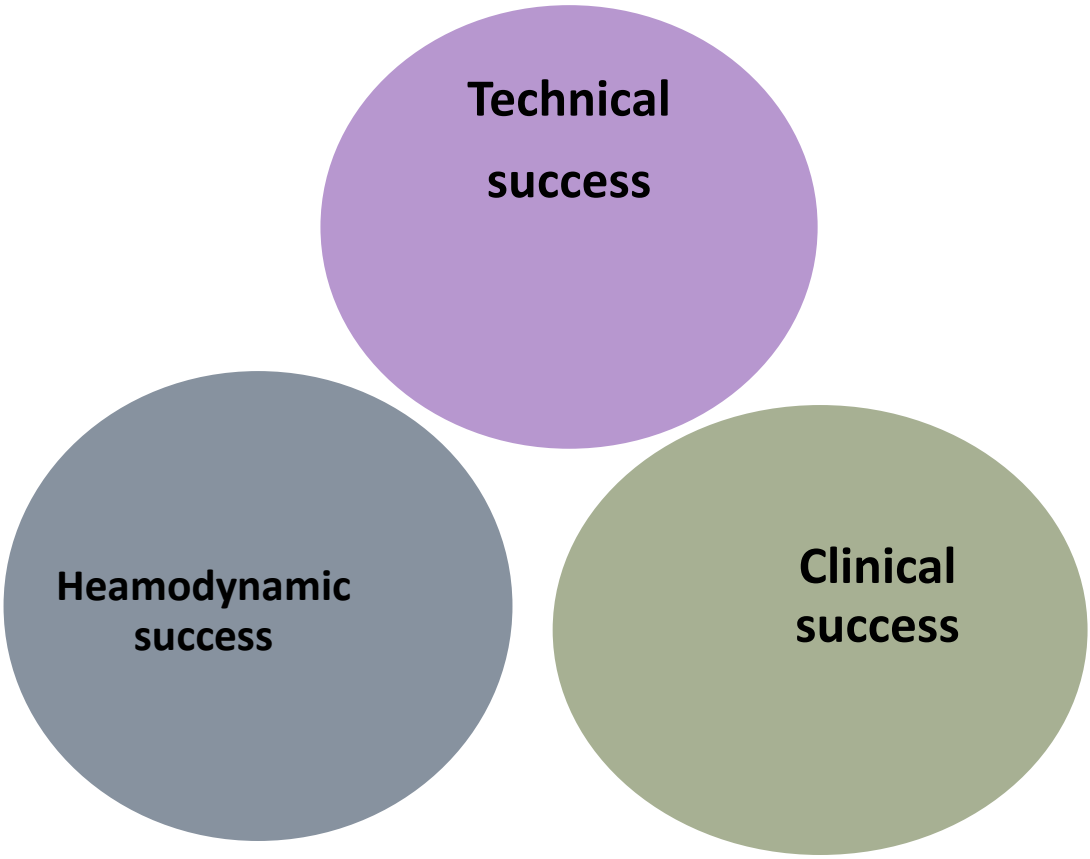
Catheter venogram and Contrast enhanced CT abdomen are other imaging modalities that can be used to asses shunt patency.

Patient with suspected shunt malfunction based on symptoms and Doppler findings undergoes catheter venogram. Absence of filling of shunt on catheter venogram suggests shunt block, with narrowing of the shunt lumen with high pressure gradient across port-systemic circulation suggests stensosis.

If the catheter venogram shows stenosis balloon angioplasty of the stent is done. In case of complete occlusion thrombolysis and thrombectomy is done.

On contrast enhanced CT abdomen, complete occlusion is seen as non-opacification of the shunt where as partial opacification suggests partial thrombosis.

Success of TIPS procedure:



Technical success: It is defined as correct creation of an intra-hepatic channel between IVC/hepatic vein and portal vein. It also includes proper placement of the stent within this channel (7).

Heamodynamic success: Heamodynamic success means decrease in the porto-systemic gradient to 12mm Hg or below it. It can also be defined as reduction of this gradient by 20% (9).

Clinical success:It is measured in terms of improvement in the clinical signs and symptoms of the patient and patency of the stent over a period of time (7).

Treatment of TIPS stenosis and TIPS occlusion:

Patients having shunt occlusion are treated with thrombectomy, thrombolysis and balloon angioplasty.

Patients with TIPS stenosis are treated with balloon angioplasty.

MATERIALS AND METHODS:

Study period:

The study was conducted in the Department of Radiology in the period between July 2016 to August 2017 after obtaining approval from the Institutional Review Board (IRB Min No 9963 dated 02/03/2016)

In this study comparison of clinical outcome and primary and secondary patency of Gore-Viatorr and Niti-S stents was conducted. All the patients who had already undergone TIPS in Department of Radiology and patients undergoing TIPS during August 2016 to July 2017 were included in this study. Data from the year of 1999 was collected and retrospectively analyzed, whereas data collected from patients undergoing TIPS during August 2016 to July 2017 was prospectively analyzed.

Study design: prospective and retrospective cross sectional descriptive study

Recruitment of subjects:

Inclusion criteria:

All the patients who have undergone TIPS procedure in the Department of Radiology, CMC Vellore from 1999 onwards were included in the study

Patients who needed TIPS or DIPS and underwent stent placement during August 2016 to July 2017 were prospectively analysed. In all these patients Niti-S stent was used as Gore Viatorr was not available in India, informed consent was taken by the principal investigator.

Patients who underwent additional placement of stent along with primary stent as

Niti-S or Gore Viatorr stents were also included in the study. Additional stent placed was Fluency stent in 3 patients.

Exclusion criteria:

Patients with severe heart failure, severe pulmonary hypertension and severe encephalopathy were excluded and did not undergo the procedure.

Patients who underwent TIPS or DIPS with primary stent other than Niti-S and Gore Viatorr stents were excluded.

Sample size calculation:

The required sample size to compare the primary patency rates across Gore Viatorr and Niti-S stents used in Transjugular intrahepatic portosystemic shunt (TIPS) was found to be 49 in each of the groups with 80% power and 5% level of significance when the expected difference in the patency rates was considered as 30%.

Formula:

Where, P1 = 77%
P2 = 50%;
Power = 80%; Level of significance = 5%

Reference for the above formula: Sahai H, Kurshid A.

Formulae and tables for the determination of sample size and power in clinical trials for testing differences in proportions for the two sample design: a review.

Statistics in Medicine, 1996; 15: 1-21.

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation

Proportion in group (primary patency rate in

Gore Viatorr0.77 0.77 0.7 0.7 0.7 0.7

Proportion in group (primary patency rate

in Niti S stents) 0.66 0.5 0.6 0.55 0.5 0.45

Estimated risk difference 0.11 0.27 0.1 0.15 0.2 0.25

Power (1- beta) % 80 80 80 80 80 80

Alpha error (%) 5 5 5 5 5 5

1 or 2 sided 2 2 2 2 2 2

Required sample size for each arm 263 49 35 6 93 60

Data collection:

All the demographic details of the patients along with indication for TIPS procedure, cause of portal hypertension and cirrhosis of liver, type, number and dimensions of stent used, presence of hypercoagulable state, post TIPS symptoms, Doppler findings, catheter venogram findings and treatment of shunt failure were collected using a questionnaire.

All the patients who had already undergone TIPS procedure all the above mentioned data was collected from the clinical work station and PACS system.

Those who underwent TIPS procedure during July 2016 to August 2017 time period informed written consent of the patient was taken before the procedure and above mentioned data was collected

TIPS Procedure:

Pre-intervention measures:

Patients having large volume ascites or hydrothorax underwent tapping. This helped in positioning the liver in a more favourable position for portal puncture. It also improved DSA image quality and reduced radiation exposure. Also improved respiratory function and helped during sedation.

Pre TIPS Imaging:

Ultrasound and Doppler examination was done to rule out portal vein thrombosis, portal cavernoma formation, hepatic vein thrombosis, hepatic arterial pathologies and liver cyst or tumour, collaterals, splenic size and ascites.

Assessment of vascular anatomy and most suitable hepatic vein was selected for the procedure, if the hepatic veins were damaged and not accessible DIPS was planned.

Laboratory tests were doneto evaluate renal and liver function, MELD score, Child Pugh classification, prothrombin time, partial thromboplastin time, INR, complete blood count, cardiac evaluation was done to rule out existing cardiac disease.

Hepatic encephalopathy was ruled out, those patients who had hepatic encephalopathy were medically managed.

Setting and location:

TIPS procedure was performed in DSA suite situated on the ground floor of main block of CMC hospital.

DSA Suite in Department of Radiology

Seimens artis zee, biplane machine

Doppler examinations were performed using Toshiba machines in room 8C, 9A, 9B and Asha Doppler room 11 in Department of Radiology, Christian medical Hospital, Vellore.

Toshiba machine in room 8C

Equipments:

18G puncture needle

Vascular sheaths 9F, 10F

0.035 inch J guide wire

TJLB cannula

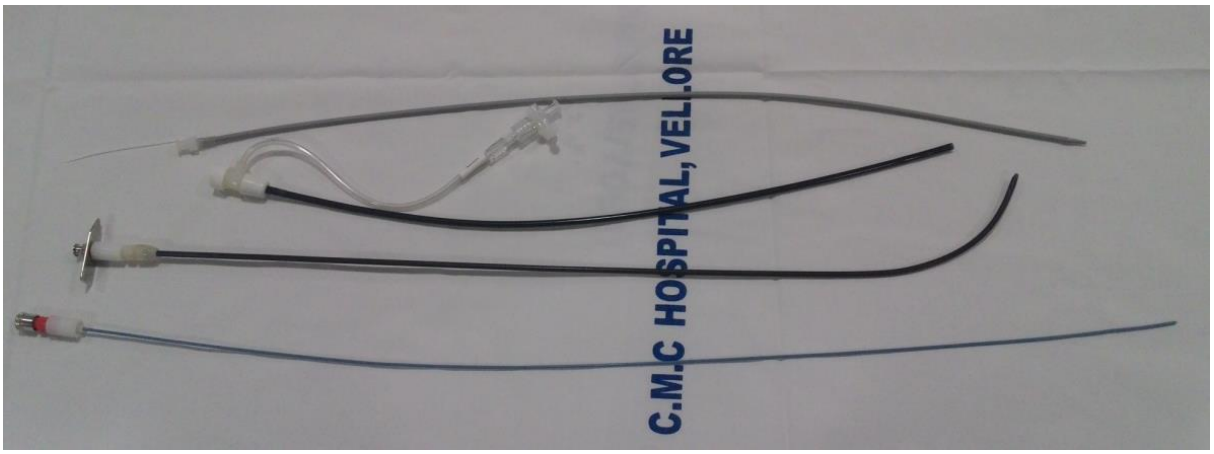
Rosch Uschida needle

Pigtail catheter, maker pigtail catheter

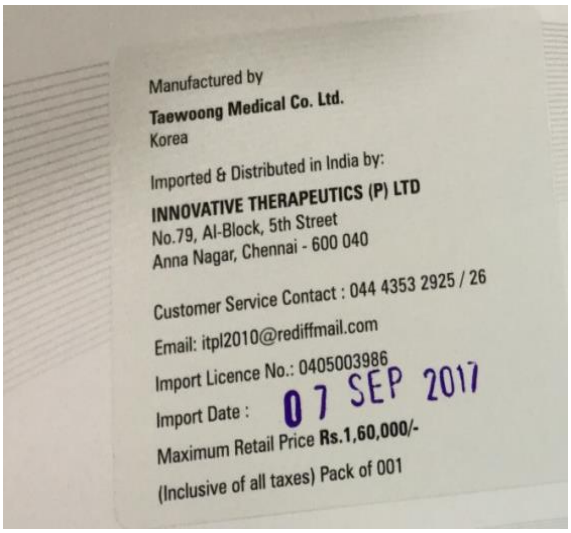
Balloon catheters

Nitis-S stent

Rosch-Uchida Transjugualr Liver access Set (Cook medical)



Niti-S stent used in our study



Technique of TIPS:

Procedure was performed in DSA suite.

It was performed using sedation or under general anaesthesia.

Using ultrasound guidance right internal jugular vein was punctured using 18G needle.

IJV access was secured with 9F sheath and then upgraded to 10F sheath.

5000 IU Heparin bolus was given during the procedure.

J guide wire (0-.035 inch) was introduced through this sheath and advanced in to the itra-hepatic IVC under fluoroscopic guidance and venography was performed using Pigtail cathter, pressure in the right atrium and IVC is measured.

TJLB cannula was introduced in to the IVC through which Rosch uchida needle was advanced in to the cannula.

Under USG guidance right hepatic vein or IVC was punctured, needle was advanced in the hepatic parenchyma and then right branch of the portal vein was punctured, marker Pigtial catheter was passed over the guide wire, venography was performed and pressure in the portal vein was measured.

Amplatz wire was passed through the marker pigtail catheter, intra-parenchymal track was dilated using balloon catheter.

Length of the required stent was measured depending upon the number of markers present over the pigtail catheter in the parenchyma. Expandable covered metallic stent was deployed within the tract, covered portion lies within the hepatic parenchyma, uncovered part of the stent which measured 2cm lies within the portal vein, this uncovered portion allows free flow of blood through interstices and prevents thrombus formation.

Balloon dilatation of the stent was done upto desirable diameter usually upto 10mm, in case of patients with hepatic encephalopathy stent is dilated upto 8mm to reduce the shunt volume

Last step was post TIPS check portogram and post TIPS pressure measurements in the portal vein and the right atrium using pigtail catheter.

Variations in procedure:

1) One patient already had IVC stent, in this patient TIPS stent was placed through the struts of the IVC stent, this is called as strutpalsty.
2) Many of the patients had two stent placements when length of one stent was not enough.
3) When right branch of portal vein was difficult to access left branch of portal vein was used.
4) Few of the patients having shunt malfunction underwent stent within stent placement when adequate recanalisation was not possible with thrombolysis, thrombectomy and balloon angioplasty

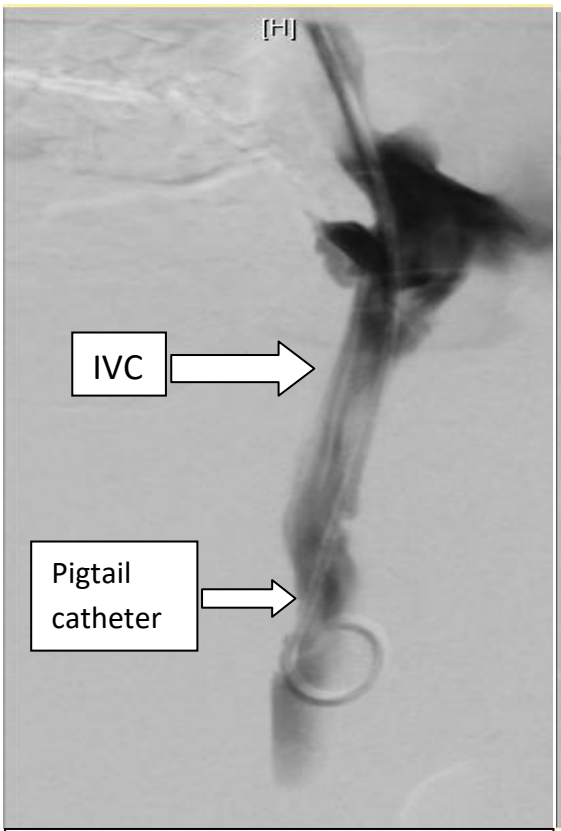


Figure 4a : showing IVC catheter venogram

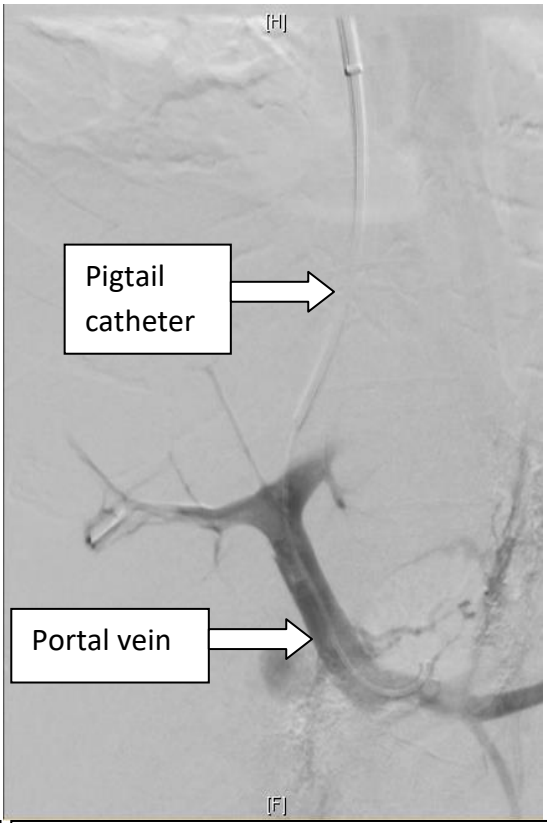


Figure 4b : showing portogram

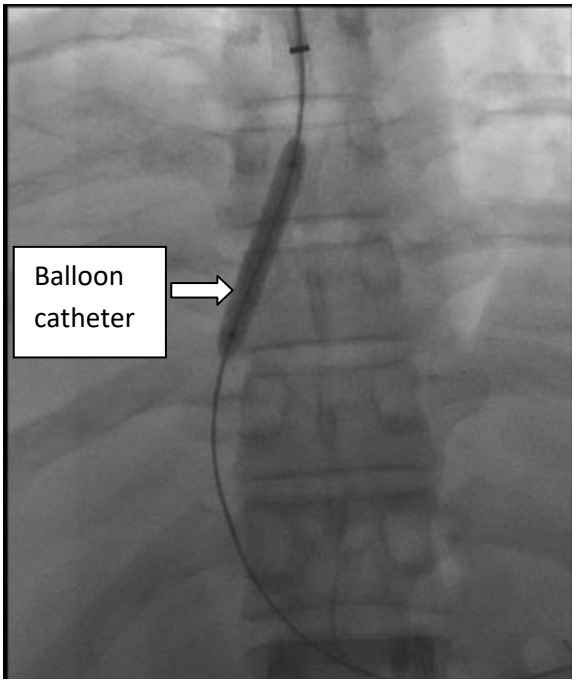


Figure 4c: showing dilatation of parenchymal tract using balloon

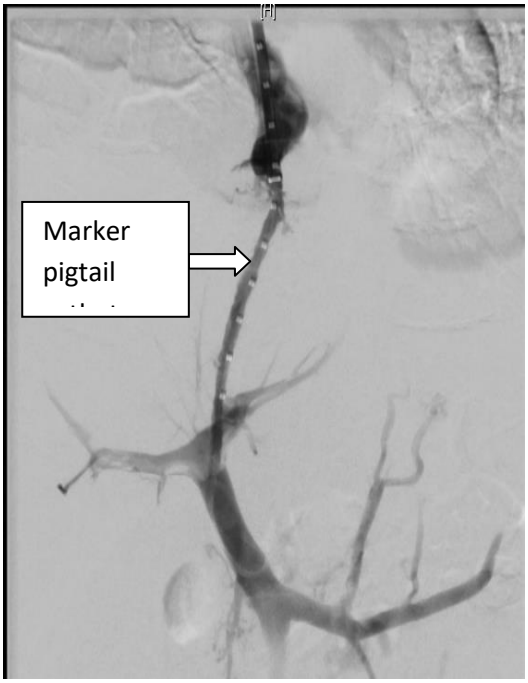


Figure 4d: showing marker pigtail insertion

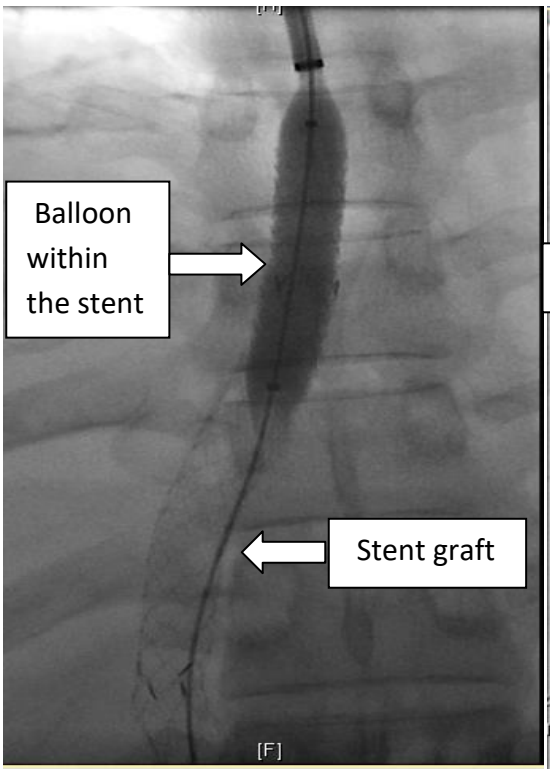


Figure 4e: showing dilatation of the deployed stent

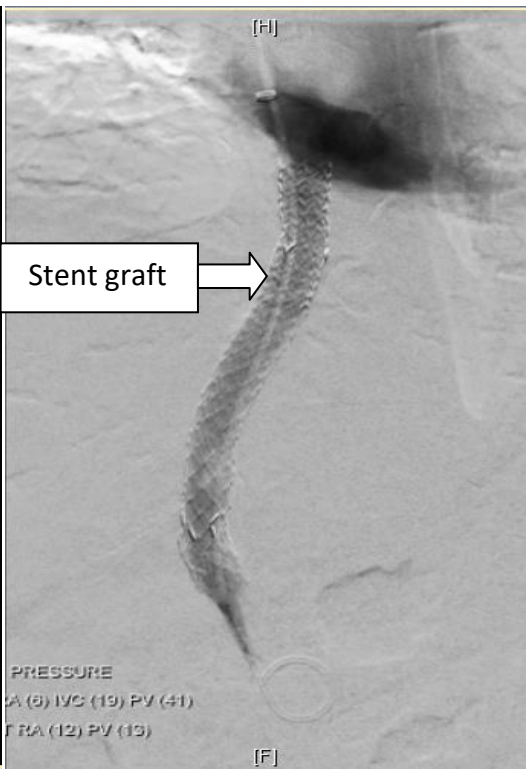


Figure 4f: showing opacification of the stent

Post TIPS follow up:

Regular follow up of these patients was done within 1week, at 1, 3, 6 months, at 1st year, every 6 monthly after 1 year.

Clinical examination and Doppler examination was part of routine evaluation.

a) Clinical outcome:

It was measured in terms of reduction of symptoms, no new symptoms, development of new symptoms and worsening of symptoms.

Shunt patency was evaluated using Doppler findings and or catheter venogram findings.

b) Doppler evaluation:

It included, whether the shunt is patent or blocked. Shunt velocities were taken at portal end, mid shunt and caval end. Velocities within 90-190 cm/sec range were considered normal. Velocities above below 90 and above 190 were considered abnormal. Main portal vein velocity above 30 cm/sec was considered normal, velocities below 30cm/sec were considered abnormal.

Increase or development of new collaterals, new appearance ascites or increase in ascites was also checked for, and if present was considered abnormal.

c) Catheter venogram:

If the patient was symptomatic and Doppler was abnormal patient underwent catheter venogram with pressure gradient measurement. If patient was symptomatic and Doppler was abnormal or if patient was asymptomatic and Doppler was abnormal patient underwent catheter venogram with pressure gradient measurement.

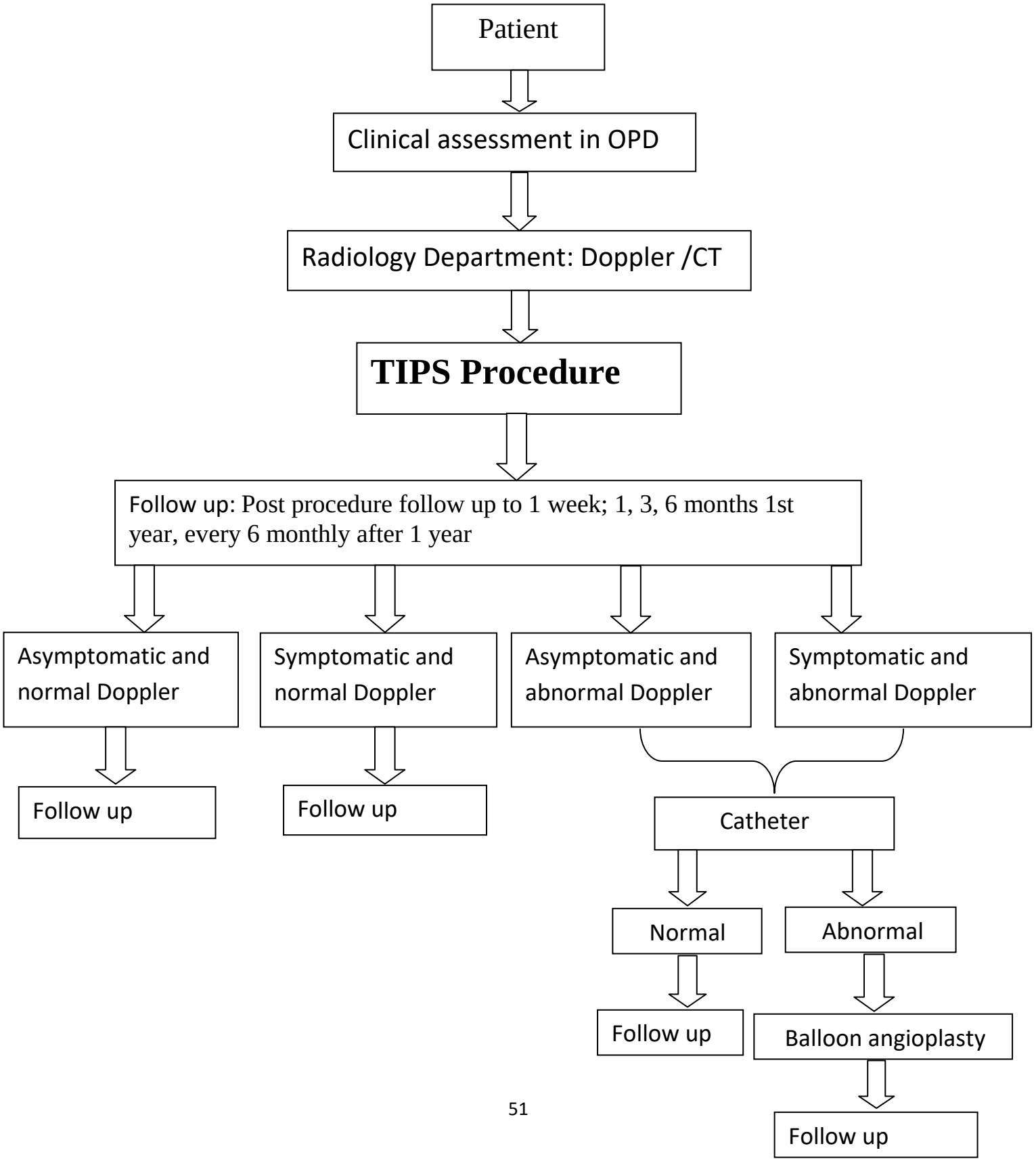
Presence of narrowing of the stent lumen with high pressure gradient was considered as shunt stenosis. Non opacification of the shunt was considered as shunt occlusion.

d) Shunt revision:

If catheter venogram findings were abnormal patient underwent balloon angioplasty. Patients with shunt occlusion were treated with thrombectomy, thrombolysis followed by balloon angioplasty. Those patients who had shunt stenosis underwent balloon angioplasty alone. Patients who showed persistent shunt narrowing even after balloon angioplasty had additional stent placement within the previously existing stent. These patients who had shunt revision were also regularly followed up.

SUMMARY OF METHODOLOGY:

Figure 5: showing summary of methodology



Statistical analysis:

Data entry was performed using Epidata Entry version 3.1, a dedicated data entry software. Statistical analysis was performed using SPSS version 20.0 software. A p value of less than 0.05 indicated statistical significance.

Discrete variables are reported as proportions.

Continuous variables are reported as Mean ± SD or median and interquartile range.

Primary patency rate and secondary patency rate was calculated using Kaplan Meier survival analysis.

Statistical significant association between two groups were calculated using Log rank test and Pearson's correlation test was used to analyze the correlation between primary patency rate of Gore-Viatorr and Niti-S stents

RESULTS

Patient characteristics:

1. **Age distribution**

Age distribution: Mean age of patients was 37.8, range was from 13 to 76 years

2. **Gender distribution:**

Amongst total number of patients 53 were males and 28 were females

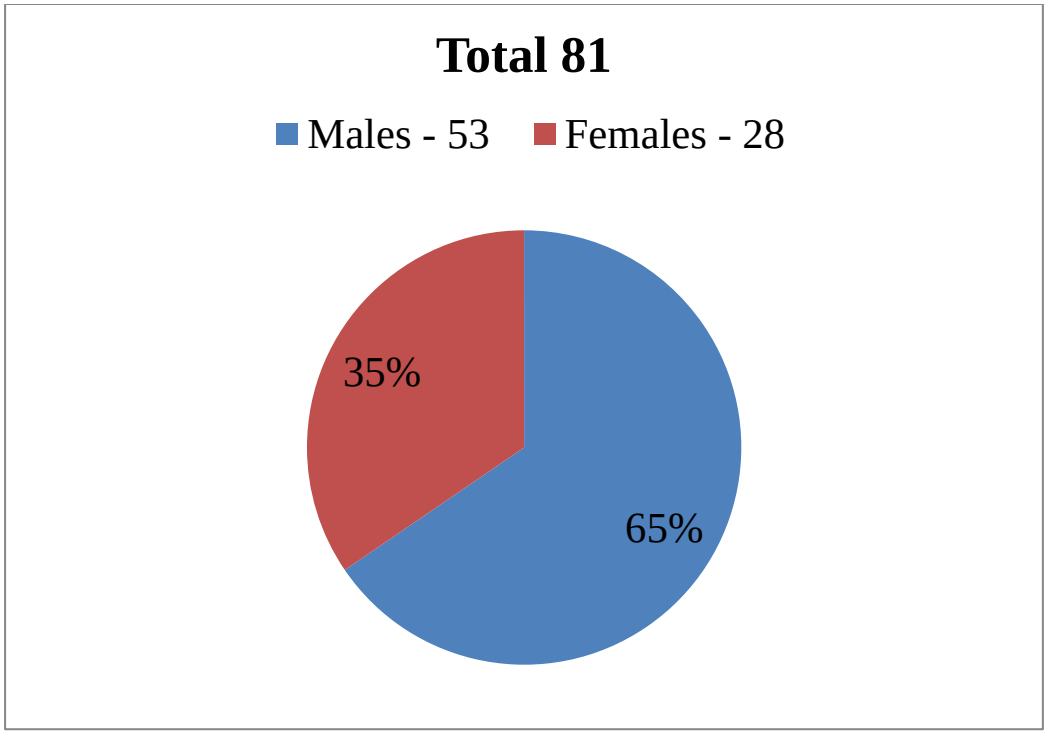


Figure 6: showing gender distribution among patients

Gender distribution among patients with Gore-Viatorr and Niti-S is shown by column chart below

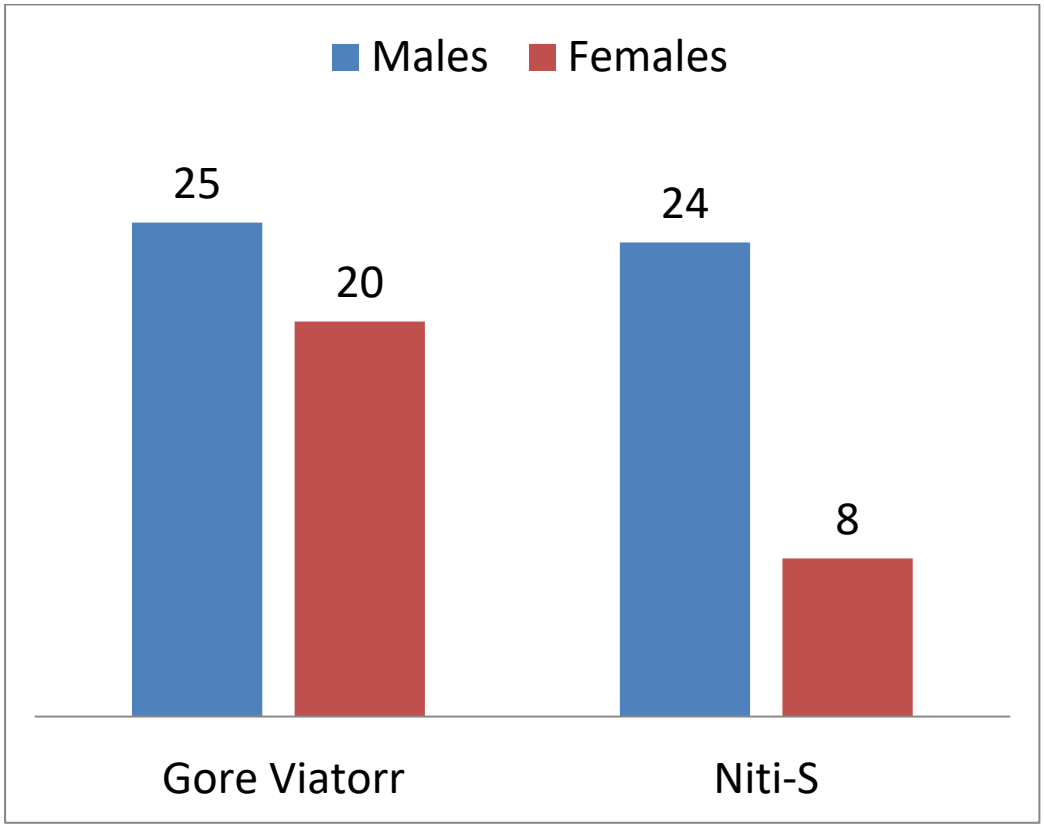


Figure 7: showing gender distribution among two groups

Amongst total 45 Gore Viatorr 25 were males, 20 were females

Amongst total 36 Niti-S patients 24 were males, 8 were females

3. Type of stent used

Out of total 81 patients, 45 patients had Gore-Viatorr and 36 patients has Niti-S stent placement.

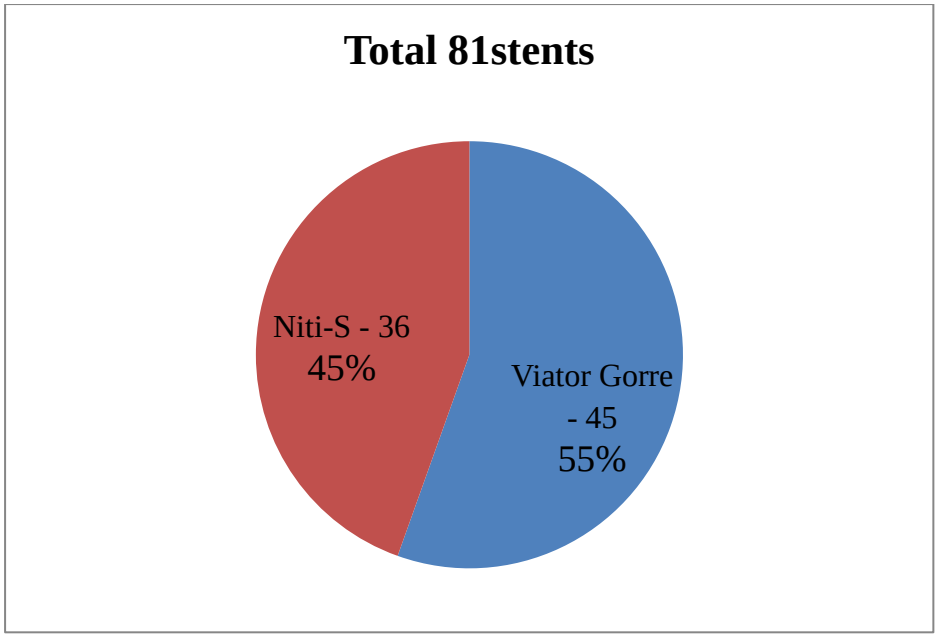


Figure 8: showing distribution of patients among each type of stent

4. Indication for TIPS/DIPS:

Most common indication for TIPS/DIPS in our study was refractory ascites. Out of total 81 patients 60 had an indication of refractory ascites contributing to 79% of cases. Second most common cause was variceal bleeding. 12 patients had an indication of variceal bleeding which accounted for 15% of cases. Bridge to liver transplant was an indication among 3 patients accounting to 3.7 % of cases. Least common indication was refractory hydrothorax. Only 2 patients had this indication which accounted for 2.5% of cases.

Indication for TIPS	Number of patients
Refractory ascites	60 (79%)
Variceal bleeding	12 (15%)
Refractory hydrothorax	2 (3%)
Bridge to liver transplant	3 (4%)

Table 2: showing distribution of indication for TIPS in all patients

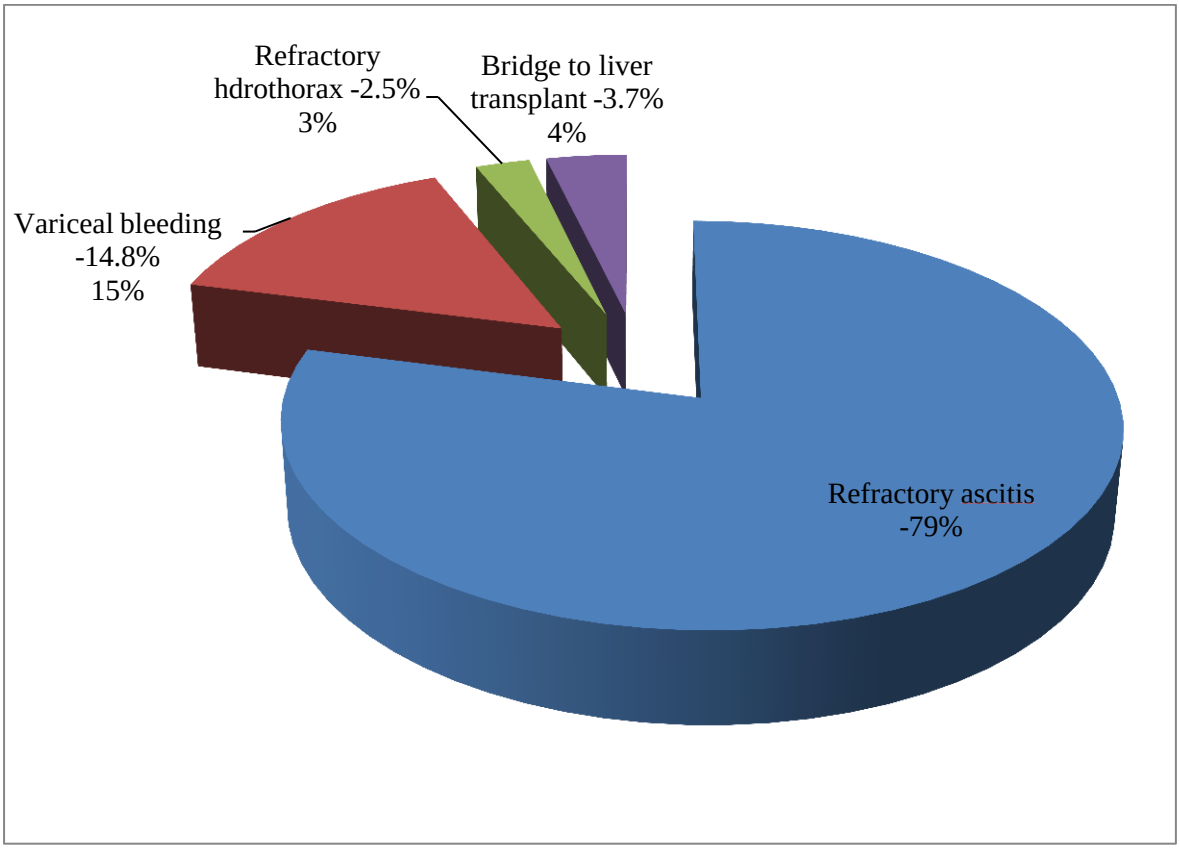


Figure 9: showing percentage distribution of indications for TIPS procedure

Most common indication for TIPS in Gore Viatorr group was refractory ascites. Out of total 45 patients of Gore Viatorr 37 patients had TIPS due to refractory ascites. Second most common cause was variceal bleeding, 7 patients had this indication. Out of remaining 2 patients 1 patient had TIPS due to refractory hydrothorax and other 1 had as to bridge to liver transplant.

Most common indication for TIPS in Niti-S was also refractory ascites. Out of total 36 patients of Niti-S 24 patients had TIPS due to refractory ascites. Second most common cause was variceal bleeding, 5 patients had this indication. Out of remaining 3 patients 1 patient had TIPS due to refractory hydrothorax and other 2 had as a bridge to liver transplant.

Indication	**Gore Viatorr (45)**	**Niti-S (36)**
Refractory ascites	36	24
Variceal bleeding	7	5
Refractory hydrothorax	1	1
Bridge to liver transplant	1	2

Table 2: showing indication for TIPS in patients with Gore Viatorr and Niti-S

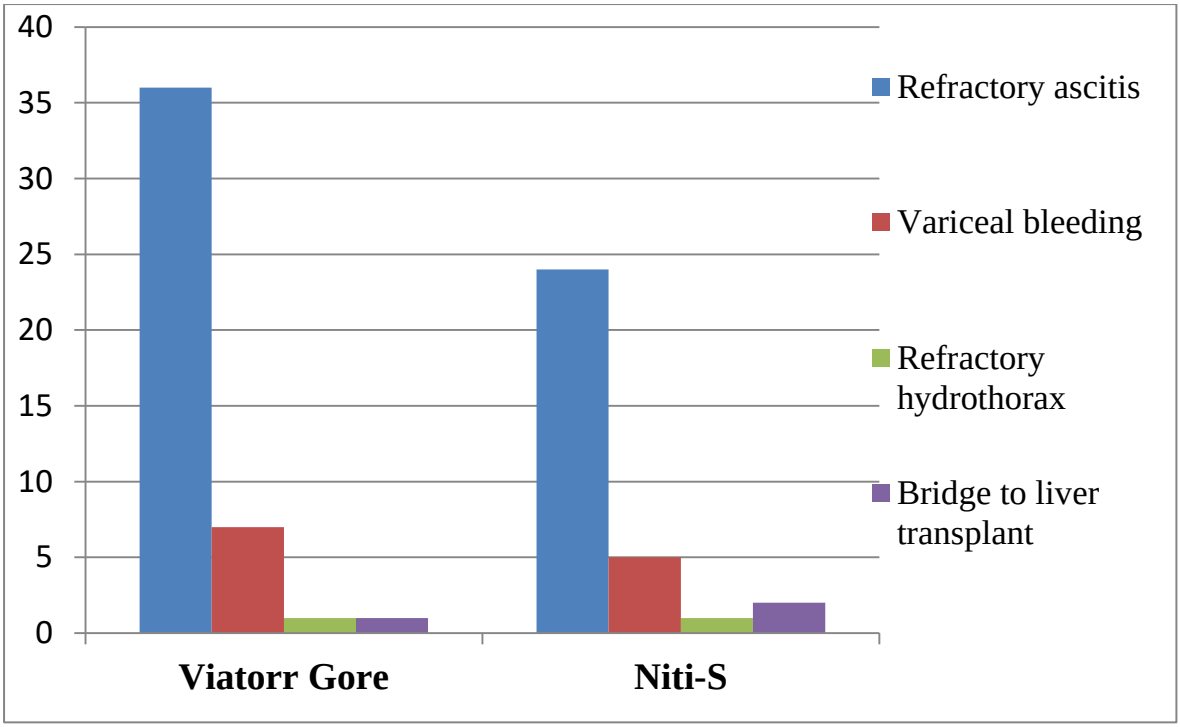


Figure 10: showing indication of TIPS procedure in Gore Viatorr and Niti-S

5) Cause of portal hypertension:

In our study most common cause of portal hypertension was Budd Chiari syndrome. Out of total 81 patients 56 had Budd Chiari. Second most common cause of portal hypertension was alcoholic liver disease. 10 patients had alcoholic liver disease. 5 had cryptogenic cirrhosis, 4 had HBV/HCV related liver disease, 3 had NAFLD (non alcoholic fatty liver disease). Non cirrhotic portal hypertension, Wilson's disease veno-occlusive disease had 1 patient each.

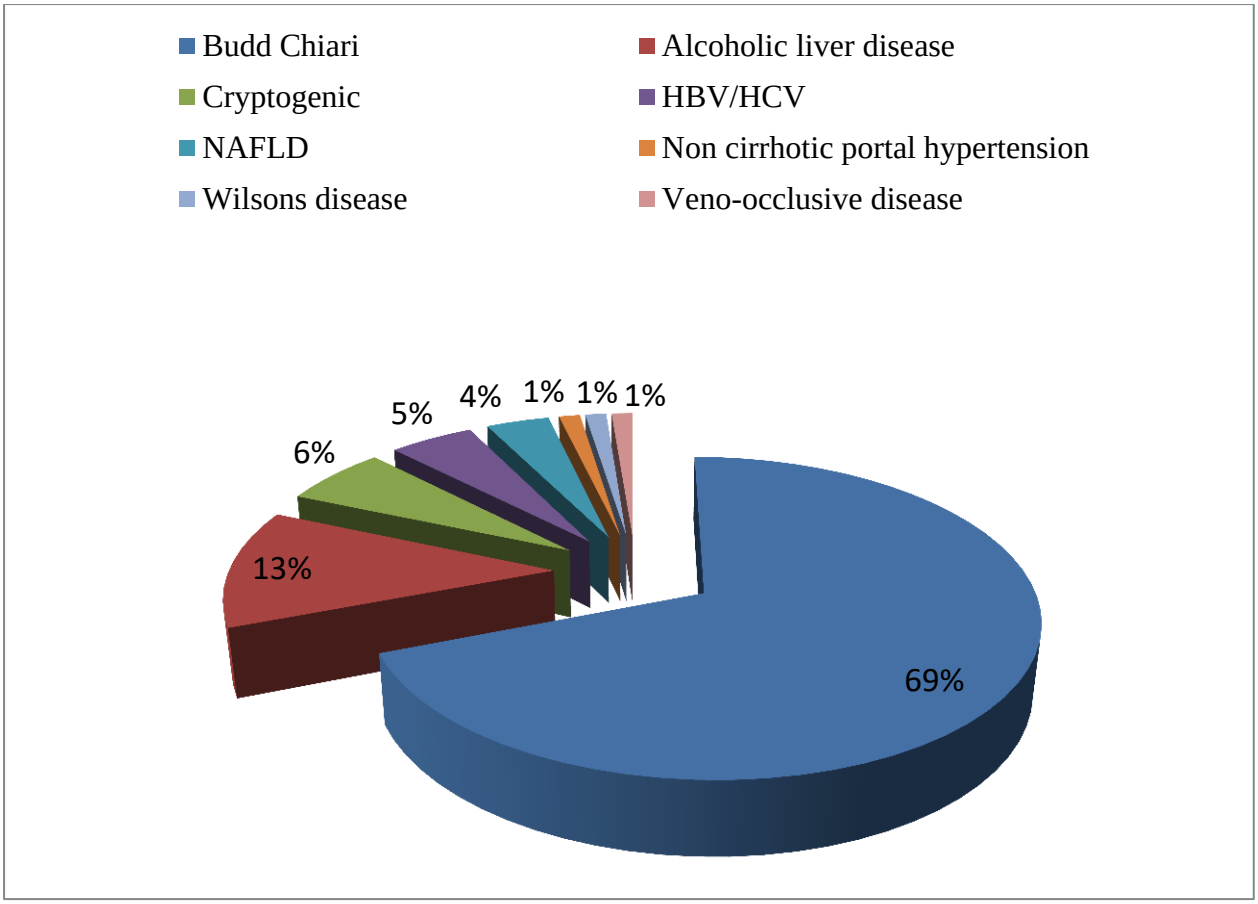


Figure 11: showing distribution of causes of portal hypertension

Cause of portal hypertension	**Total number of patients**
Budd Chiari syndrome	56 (69%)
Alcoholic liver disease	10 (13%)
HBV/HCV infection	4 (5%)
Cryptogenic cirrhosis	5 (6%)
NAFLD	3 (4%)
Non cirrhotic portal hypertension	1 (1%)
Wilsons disease	1 (1%)
Veno-occlusive disease	1 (1%)

Table 3: showing distribution of causes of portal hypertension

Cause of portal hypertension	**Gore Viatorr(45)**	**Niti-S (36)**
Budd Chiari syndrome	33 (73%)	23 (63.8%)
Alcoholic liver disease	3 (6.6%)	7 (19%)
HBV/HCV infection	1 (2%)	3 (8%)
Cryptogenic cirrhosis	3 (6%)	2 (5%)
NAFLD	2 (4%)	1 (2%)
Non cirrhotic portal hypertension	1 (2%)	0 (0%)
Wilsons disease	1 (2%)	0 (0%)
Veno-occlusive disease	1 (2%)	0 (0%)

Table 3: showing cause of portal hypertension in patients with Gore Viatorr and Niti-S stent.

Most common cause of portal hypertension in Gore Viatorr group of patients was Budd Chiari syndrome. 33 out of 45 patients had Budd Chiari syndrome accounting for 73% of cases. Second most common causes of portal hypertension were cryptogenic cirrhosis and alcoholic liver disease having 3 patients each accounting for 6.6% of cases. Remaining causes were NAFLD (non alcoholic fatty liver disease) accounting for 2 cases and other causes like HBV/HCV related liver disease, non-cirrhotic portal hypertension and veno-occlusive disease had 1 patient each.

Most common cause of portal hypertension in Niti-S group of patients was Budd Chiari syndrome. 23 out of 36 patients had Budd Chiari syndrome. Second most common causes was alcoholic liver disease accounting for 7patients. Cryptogenic cirrhosis had 2 patients and NAFLD (non alcoholic fatty liver disease) had 1 patient.

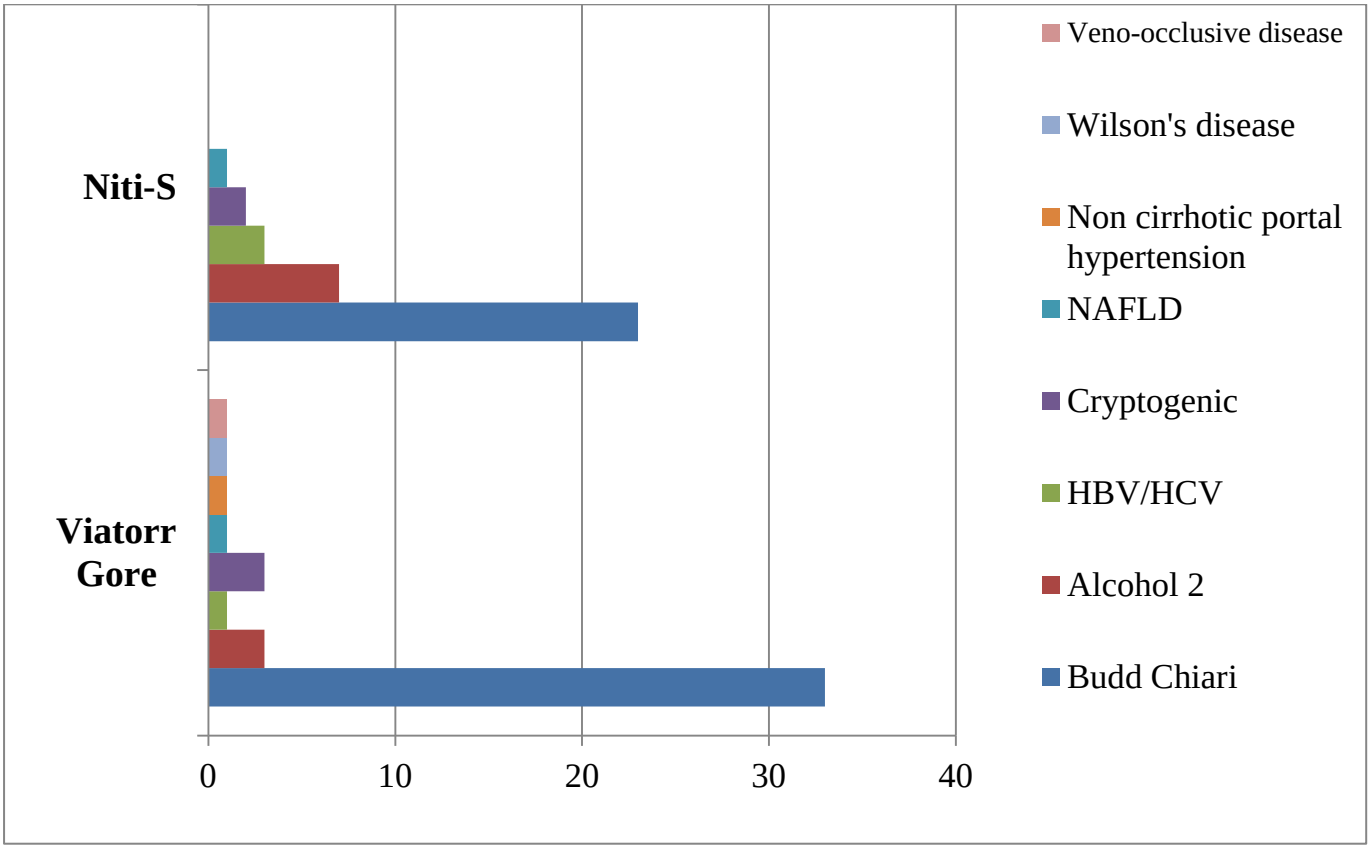


Figure 12: showing distribution of causes of portal hypertension among two groups

6) Stent dimensions:

In our study mean length of the stent was 8.9 cm (+/-2 cm), minimum length of the stent was 4cm and maximum length was 12cm.

Amongst the Gore Viatorr mean length of the stent was 8.2 cm(+/-2 cm), minimum length of the stent was 4cm and maximum length was 10cm.

Amongst the Niti-S patients mean length of the stent was 9.7 cm(+/-2 cm), minimum length of the stent was 6cm and maximum length was 12cm.

All the stents had a diameter of 10mm.

7) Outcome:

Outcome was measured in terms of technical success, heamodynamic success and clinical success.

Technical success:

Technical success was defined as correct creation of a shunt with successful placement of stent within the channel.

All the patients had a successful TIPS procedure with technical success rate of 100%.

Hemodynamic success:

Heamodyamic success was defined as decrease in the porto-systemic gradient to 12mm Hg or below or reduction of this gradient by 20% and was achieved in 100% of cases.

Mean pre TIPS pressure gradient was 21.6 +/- 0.6 mm of Hg

Mean post TIPS pressure gradient was 8.4 +/- 0.4 mm of Hg

Mean reduction in the pressure gradient 13. 2 +/- 2 mm of Hg

Clinical success:

It was defined as improvement in the clinical signs and symptoms of the patient and patency of the stent over a period of time.

Patency of shunt was determined in terms of Doppler findings, catheter venogram findings, shunt blockage and number of shunt revisions required.

Clinical findings:

Out of total 81 patients, 18 had development of new symptoms or worsening of symptoms at varying time interval, 9 belonged to Gore Viatorr and 9 belonged to Niti-S group, remaining 43 patients showed improvement in the clinical symptoms over a varying time period of 1 month to 11 years, 20 patients were lost to follow up after 1 week of post TIPS. Out of the total 18 patients who had symptoms 7 developed recurrence of symptoms after first revision of the stent, remaining 11 patients remained asymptomatic during their follow up.

Out of the 18 patients, 16 had refractory ascites and 2 had variceal bleeding. All the 9 patients in Gorre Viatorr group had refractory ascites which showed development of ascites after a symptom free period varying from 3 months to 4.3 years.

In the Niti-S group, 7 patients had refractory ascites and 2 had variceal bleeding. Out of the 7 patients 4 died within 30 days post TIPS, 1 had development of ascites after symptom free time of 7 months and recurrence of symptoms at varying intervals needing atleast 6 shunt revisions, he was not evaluated for hypercoagulable state. Remaining 2 patients were followed up for 1 year and do not have any symptoms

during this time period. One patient with variceal bleeding had pain in abdomen on day 5 of TIPS, imaging showed shunt occlusion was treated for same. Other patient with variceal bleeding developed abdominal distension 7 month post TIPS, in this time period he had no episode of variceal bleed, on evaluation he was found have hypercoagulable state.

Out of 18 patients with shunt malfunction 16 had Budd Chiari syndrome, 1 had alcoholic liver disease and 1 had cryptogenic fibrosis as a cause of portal hypertension. Out of the 9 Gore Viatorr patients, 8 had Budd Chiari syndrome and 1 had cryptogenic cirrhosis. Out of 9 Niti-S group of patients 6 had Budd Chiari syndrome and 2 had alcoholic liver disease as a cause of portal hypertension.

Out of the 18 patients with shunt malfunction 4 had hypercoagulable state and all these 4 patients had Budd Chiari as a cause of portal hypertension, rest 14 patients were not evaluated for underlying hypercoagulable state. Out of these 4, Gore Viatorr had 2 and Niti-S group had 2 patients each. One of the Gore Viatorr group patient had multiple shunt blocks and needed 3 revisions, remaining one patient was lost to follow up after 1 week of TIPS revision. Both patients in Niti-S group were symptom free for 1 year and 2 years respectively post TIPS revision.

Doppler findings:

Out of the total 81 patients 18 had shunt malfunction, 11 had shunt occlusion and remaining 8 had shunt stenosis according to the Doppler criteria defined in our study.

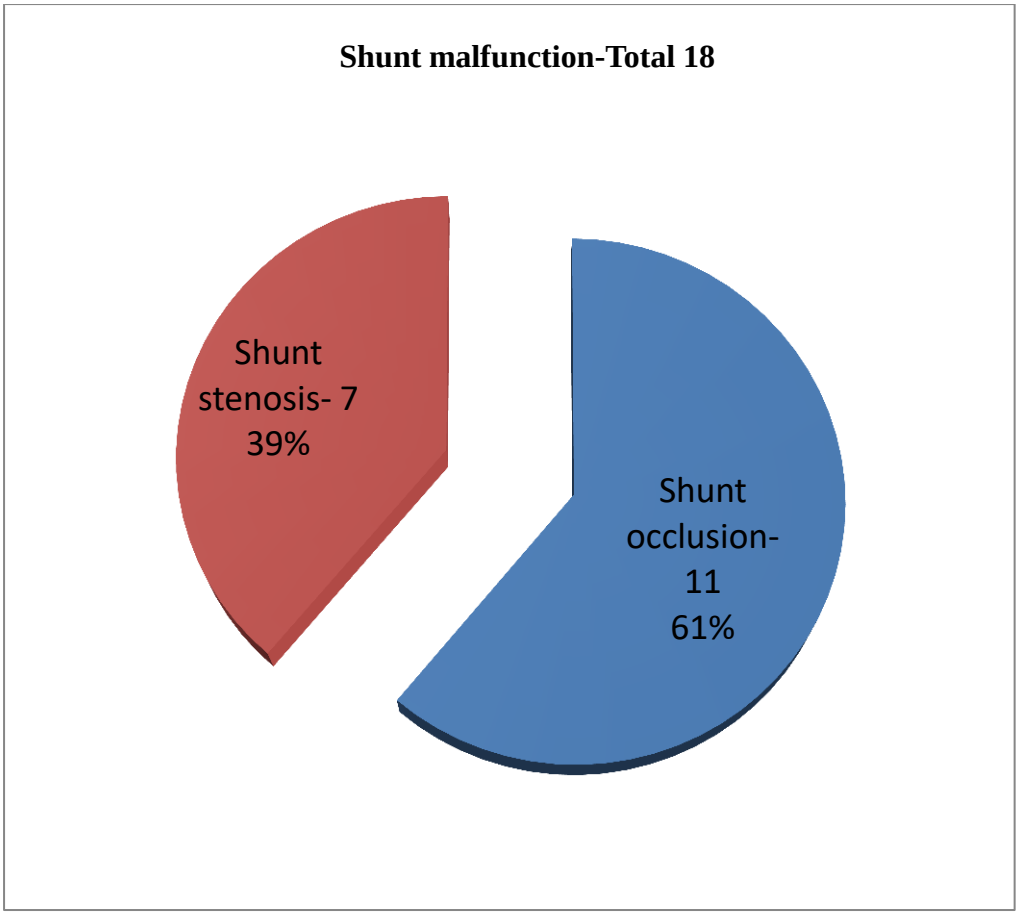


Figure 13: showing distribution of patients in causes of shunt failure

Stent type	Shunt occlusion	Shunt stenosis
Gore Viatorr	**4**	**5**
Niti-S	**7**	**2**

Table 4: showing distribution of causes of shunt failure among each group

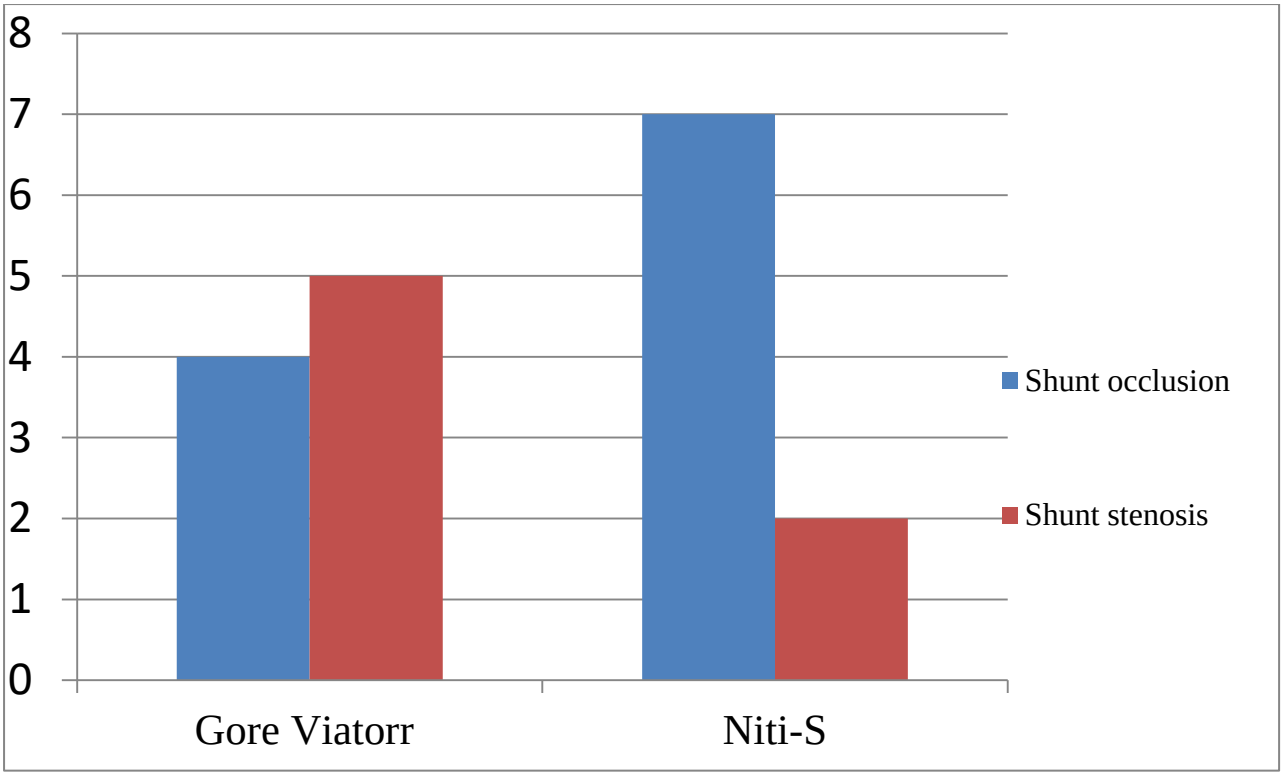


Figure 14: showing distribution of causes of shunt failure among each group

Total 7 patients who had shunt stenosis 5 belonged to Gore Viatorr group and 2 belonged to Niti-S group.

Amongst the Gore Viatorr group of patients 3 patients had abnormally high shunt velocity, 1 patient had abnormally low shunt velocity and 1 patient did not have documentation of velocities before catheter venogram. Abnormally high shunt velocities were seen at portal end and at caval end. 2 patients had high shunt velocities at portal end and 1 had at caval end. Two patients had shunt velocities more than 210 cm/sec and 1 had velocity more than 184cm/sec. All these patients had these high velocities on two follow ups during 6 month, 1 year and 2 years respectively. On the third follow when they developed symptoms, they underwent catheter venogram, findings were confirmed on catheter venogram and patients underwent balloon

angioplasty. Patient with low velocity had showed low velocities at all the 3 parts of the shunt and were below 80 cm/sec at 1 year but was asymptomatic, on follow at 2 years post TIPS his velocities remained persistently low but at this time he had developed new symptoms. This patient underwent catheter venogram, showed narrowing at caval end and underwent shunt revision.

Of the total 11 patients who had shunt occlusion 4 belonged Gore Viatorr group and 7 belonged to Niti-S group. These patients showed absence of colour flow and absence of on spectral waveform on Doppler examination. Amongst the Gore Viatorr group, patients developed shunt occlusion between 1 year to 3 years time period. Among the Niti-S group 4 out of 7 patients developed shunt occlusion in less than 20 days and remaining 3 developed over a period of 6 months to 1 year period.

Doppler images of a patient with development of new symptoms in the form of abdominal distension post TIPS

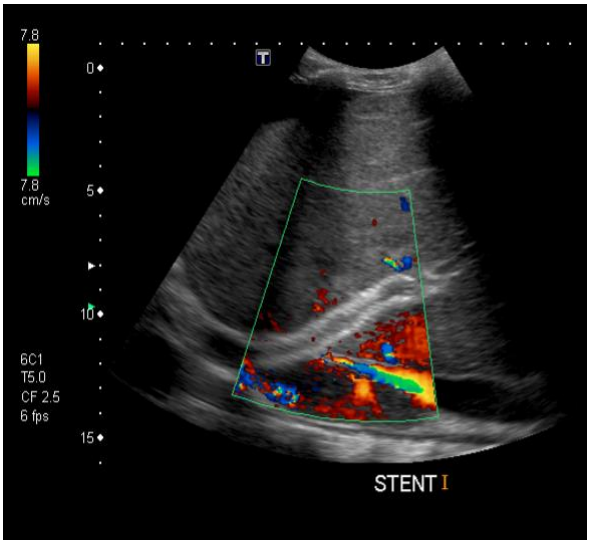


Figure 15a: showing absence of colour flow within the stent suggestive of shunt occlusion

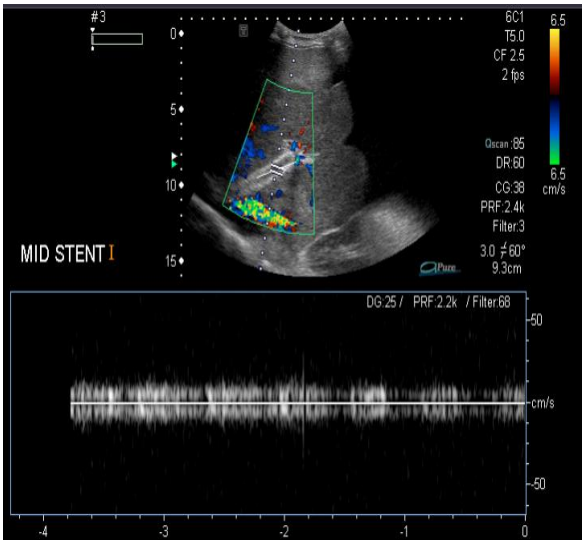


Figure 15b: showing absent spectral wave from with artifactual flow within the stent

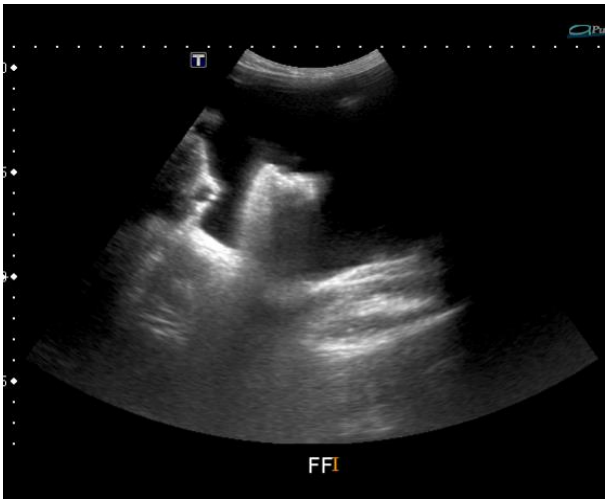


Figure 15c: showing significant ascites

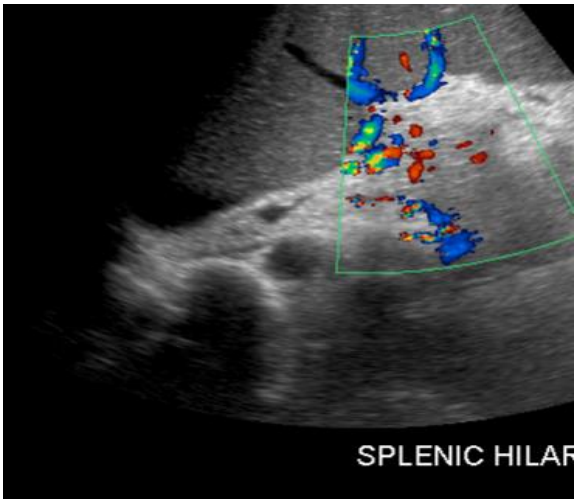


Figure15d: showing multiple splenic hilar collaterals

Absence of colour flow within the stent, absent spectral waveform, presence of significant ascites and development of new splenic hilar collaterals all these findings are suggestive of shunt occlusion. Following this patient underwent catheter catheter venogram.

Catheter venogram

Figure 15d: showing non opacification of the shunt

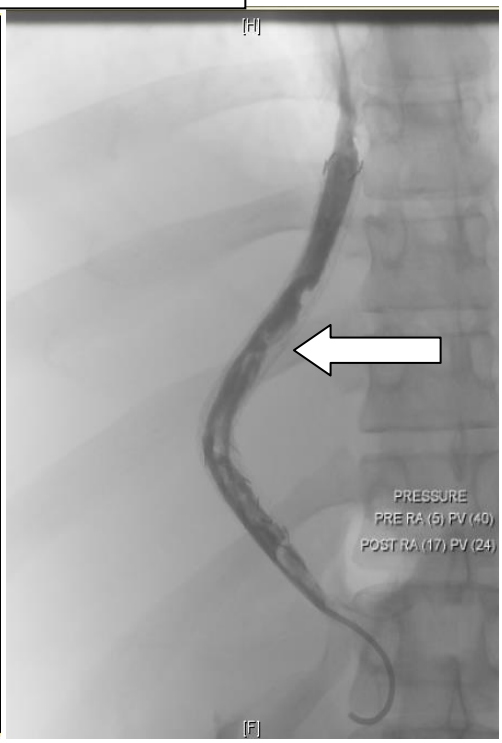


Figure 15e: showing opacification of the shunt post thrombolysis and

Catheter catheter venogramconfirmed shunt occlusion, patient underwent thrombectomy, thrombolysis and balloon angioplasty (BA).After the procedure patient had regular follow up.

Doppler images of a patient with worsening of symptoms in the form of increasing abdominal distension post TIPS

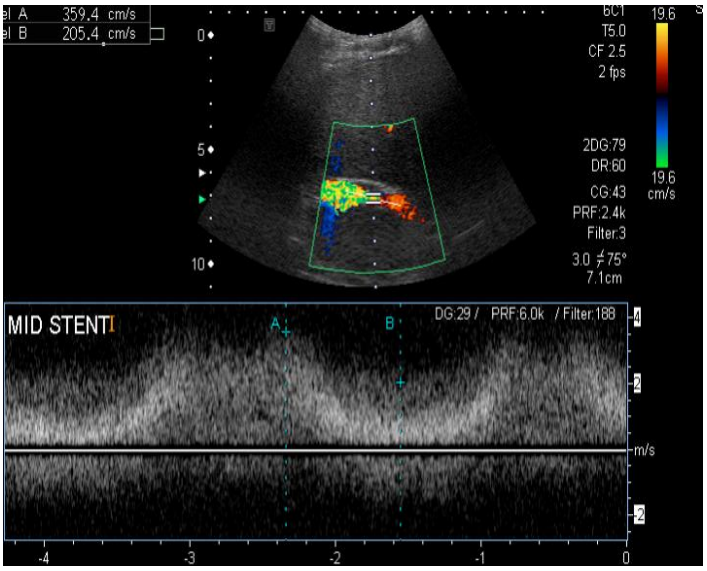


Figure 16a: showing focal narrowing of the mid part of the stent

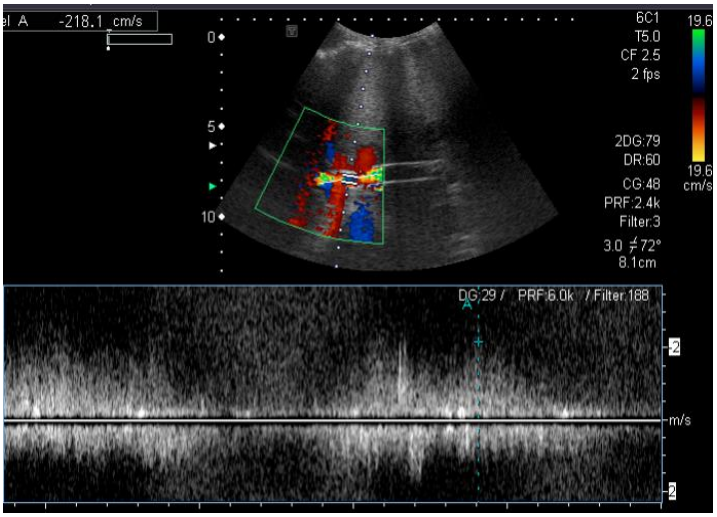


Figure 16b: showing abnormally high velocity (218 cm/sec) within the narrowed stent segment

This patient had catheter catheter venogram which confirmed the findings of the Doppler.

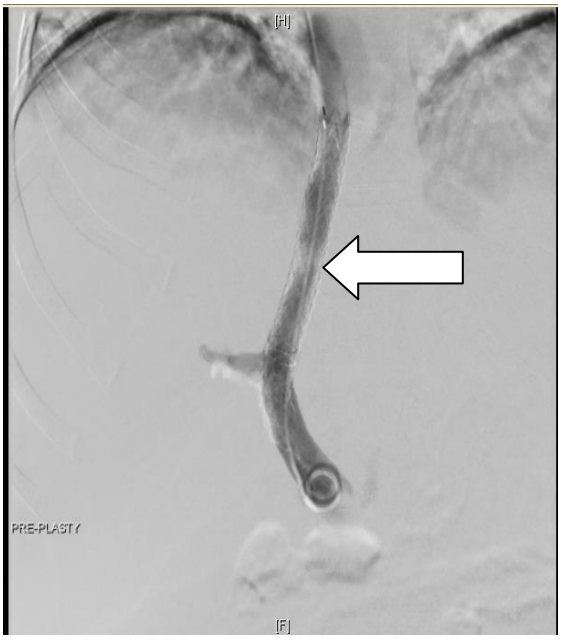


Figure 16c: showing focal filling defect in the mid part of the stent

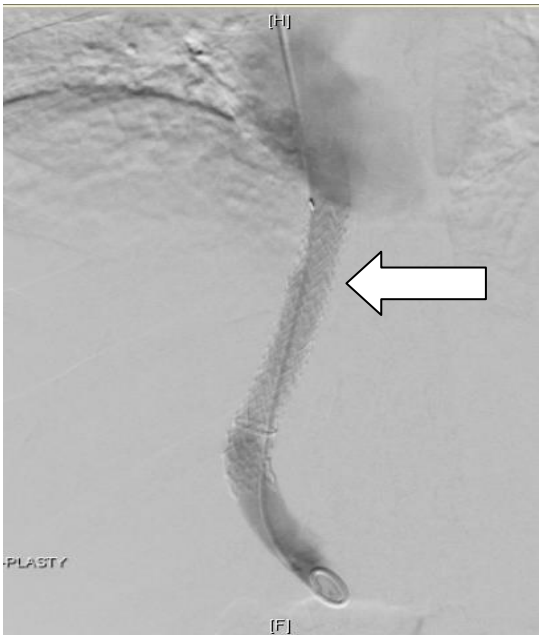


Figure 16d: showing normal opacification of the stenosed segment post balloon angioplasty

Shunt patency:

Primary patency rate was defined as duration of stent patency without revision.

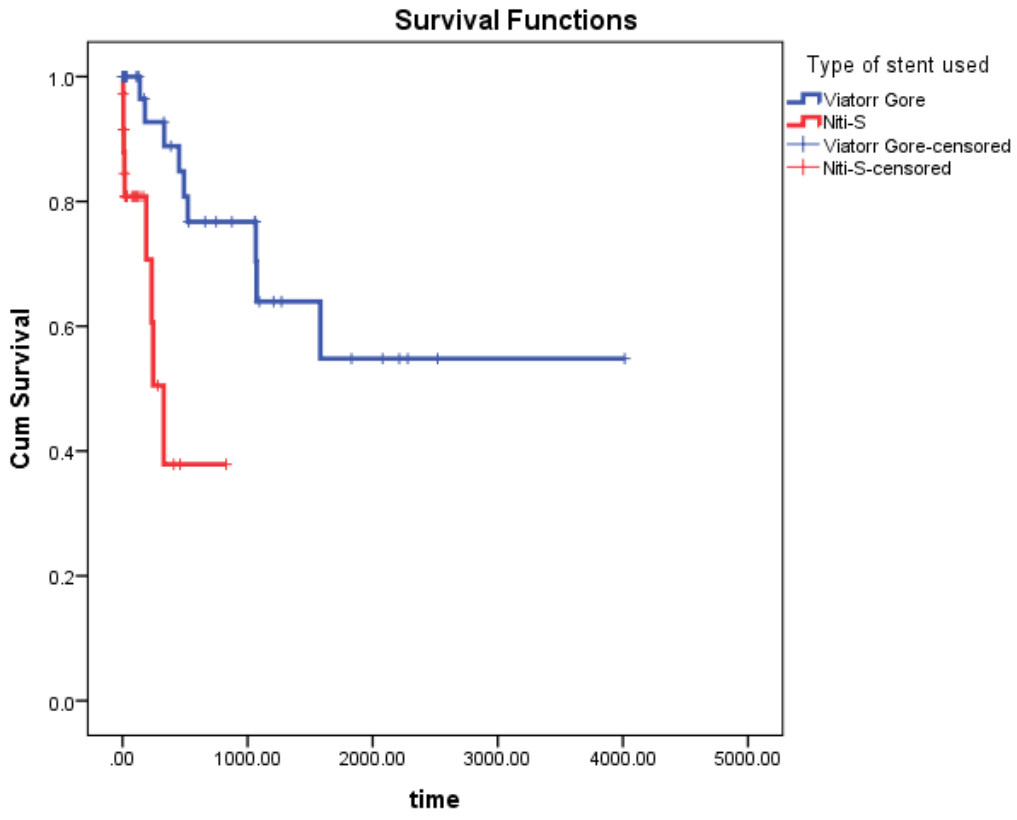
Secondary patency rate was defined as duration of stent patency after first revision.

Primary patency rate and secondary patency rate was calculated using Kaplan Meier survival analysis.

Statistical significant association between two groups were calculated using Log rank test.

Primary patency rate:

Figure 17: Kaplan Meier curve for primary patency rate



Time (in months)	Types of Stents				P value
	Gore Viatorr		Niti-S		
	Primary patency rate %	Standard error (SE)	Primary patency rate %	Standard error (SE)	
3 months	96.4	0.035	80.8	0.071	**<0.001**
6 months	92.7	0.050	70.7	0.113	
9 months	88.9	0.061	70.7	0.113	
12 months	88.9	0.061	50.5	0.145	
24 months	76.7	0.084	37.9	0.154	

Table 5: showing primary patency rates of Gore Viatorr stent at various intervals

Primary patency rate of Gore Viatorr stent at 3 month, 6 month, 9 month, 1 year and 2 years were 96.4%, 92.7%, 88.9%, 88.9%, 76.7% respectively.

Primary patency rate of Niti-S stent at 3 month, 6 month, 9 month, 1 year and 2 years were 80.8%, 70.7%, 70.7%, 50.5%, 37.9% respectively.

Mean follow time for Gore Viatorr patients was 7 years +/- 1 year.

Mean follow time for Niti-S patients was 1.1 years +/- 2 months.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	12.579	1	.000
Tarone-Ware	12.499	1	.000

Table 6: comparing association between primary patency rates of Gore Viatorr and Niti-S

Association between two groups was calculated using Log rank method which showed p value of < 0.001 at all intervals ie at 3 month, 6 month, 9 month, 1 year and 2 years suggesting the there is significant difference between primary patency rates of Gore-Viatorr and Niti-S stent at all calculated intervals.

Secondary patency rate:

In our study out of total 81 patients 18 patients developed shunt malfunction in the form of shunt stenosis or shunt blockage.

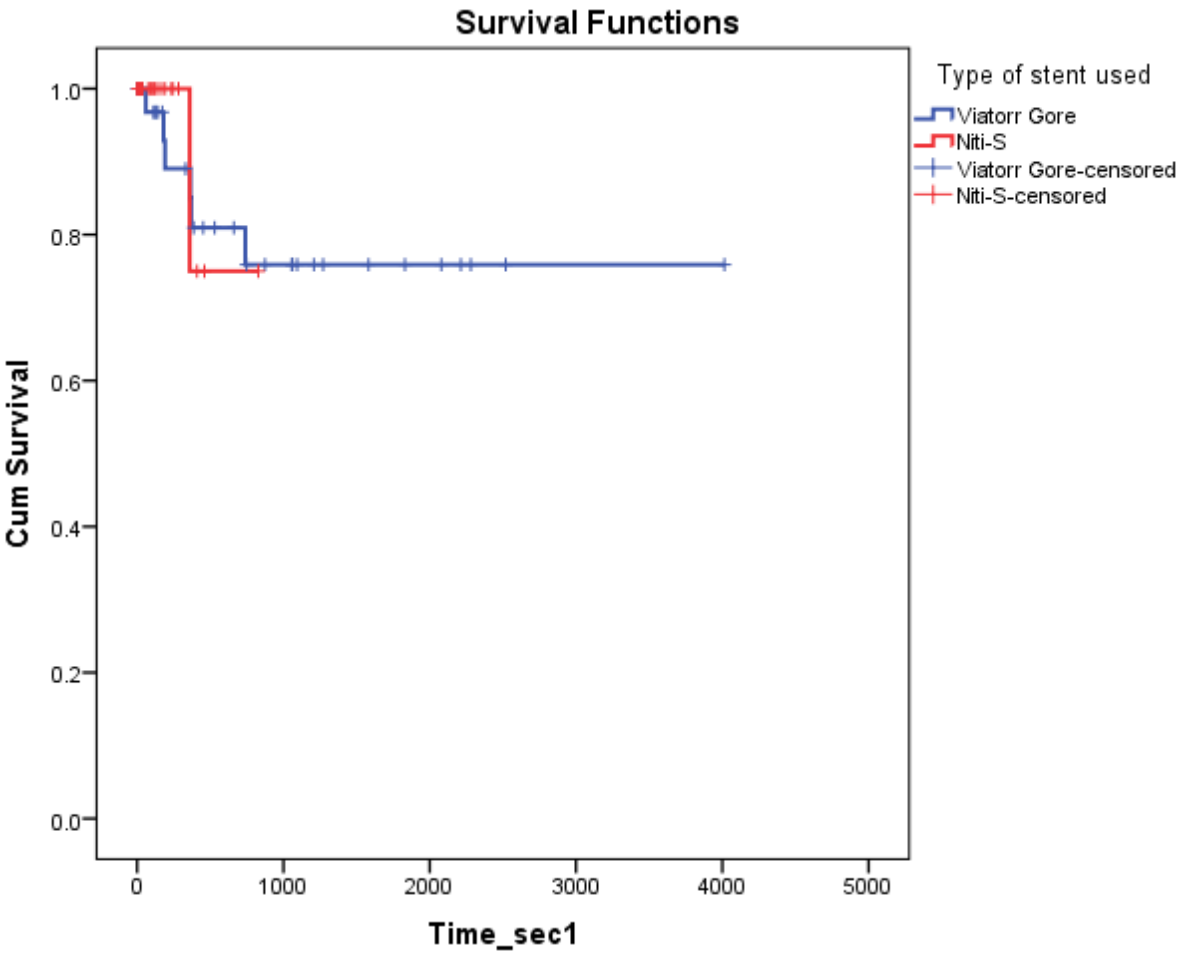
Out of these 18 patients 9 had Gorre Viatorr and 9 had Niti-S stent placement. Out of 9 patients which underwent first balloon angioplasty, 6 had one or more incidences of shunt malfunction during the follow up period and needed additional shunt revisions.

Only one out of 8 patients of Niti-S developed 2nd incidence of shunt malfunction. This patient needed 6 shunt revisions. 4 patients died within 15 days post TIPS. 3 patients who were followed up for approximately 1 years post TIPS did not have shunt malfunction during the follow up period.

Mean follow time for Gore Viatorr patients was 8.57 years +/- 8 months.

Mean follow time for Niti-S patients was 1.9 years +/- 3 months.

Figure 18: Kaplan Meier curve for secondary patency rate



Time (in months)	Types of Stent				P value
	Gore Viatorr		Niti-S		
	Secondary patency rate **%**	Standard error **(SE)**	Secondary patency rate **%**	Standard error **(SE)**	0.230
3	96.9	0.032	-	-	
6	92.9	0.049	-	-	
9	89.0	0.060	-	-	
12	85.8	0.077	75	0.02	
24	75.9	0.087	75	0.02	

Table 8: showing secondary patency rates of Gore Viatorr at various intervals

Secondary patency rates of Gore-Viatorr at at 3 month, 6 month, 9 month, 1 year and 2 years were 96.9 %, 92.9%, 89%, 85.8%, 75.9% respectively.

Secondary patency rates of Niti-S stent at 1 year and at 2 years was 75%.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.077	1	.781
Tarone-Ware	.147	1	.702

Table 9: showing association between secondary patency rates of both groups

Though the Log rank test did not show any statistical difference between the secondary patency rates of two stents and p value was more than 0.005.

Thus statistically it suggests that there is no significant difference between the secondary patency rates of both stents.

Mortality:

In our study total 7 deaths were documented. 5 out of these 7 deaths occurred in less than 30 days post TIPS. Remaining 2 deaths occurred in 2^{nd} year and 4^{th} year post TIPS respectively.

Amongst these 7 deaths, 3 patients had Gore Viatorr stent placement and 4 had Niti- S stent placement.

Those patients who had Gore Viatorr stent, one death was documented on day 4 post TIPS. This patient had underwent emergency TIPS for acute variceal bleeding, developed hypotension during the procedure, on day 2 he had worsening liver function which was thought to be due to liver infarction, day 4 he developed malena, during this period shunt was patent on Doppler evaluation, he succumbed to the illness on day 4 post TIPS. 2 deaths occurred in 2^{nd} year and 4^{th} year post TIPS respectively cause of which is not known as these patients did not follow up in our hospital and outside documents are not available.

All the 4 deaths in patients with Niti-S occurred in first 30 days post TIPS. One patient developed intestinal obstruction and one developed gangrene bowel during post op 1st week for which they were operated, developed sepsis in post op period and succumbed to the illness. One of the patient developed spontaneous bacterial peritonitis and acute kidney injury. The other patient developed hypotension during the procedure, continued to remain unstable post op and died on day 2 post TIPS.

Post TIPS survival rate:

It was defined as time taken for death of the patient after the procedure.
It was calculated using Kaplan Meier curve for both group of patients.
In our study there was no statistical difference between the two groups suggesting that post TIPS survival rate was similar for both groups.

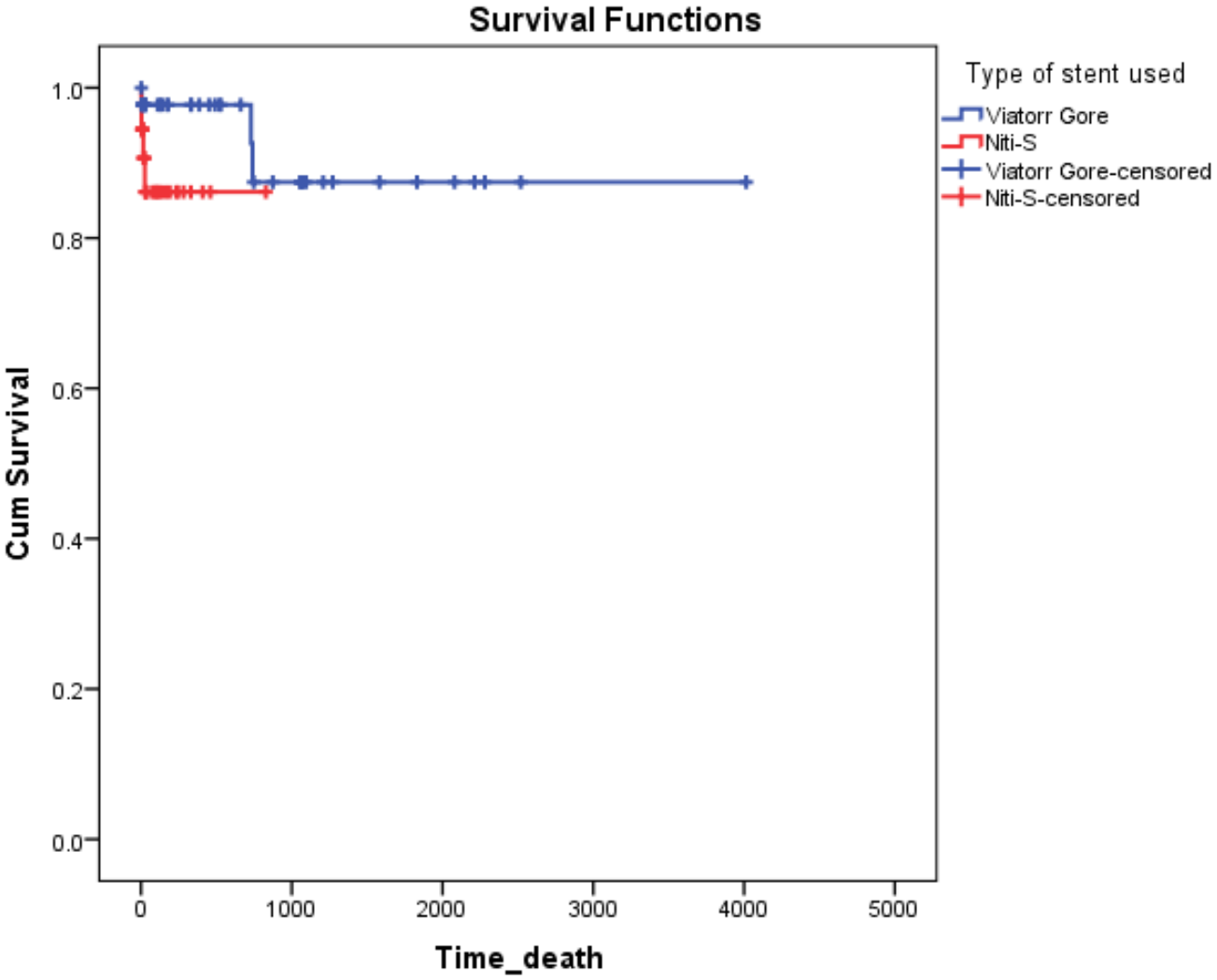


Figure 20: Kaplan Meier curve showing survival rate in Gore Viatorr and Niti-S groups of patients.

Time	Types of Stents			
	Gore Viatorr		**Niti-S**	
	Survival rate **%**	Standard error **(SE)**	Survival rate **%**	Standard error **(SE)**
3month to 1 year	97.9	0.02	86	0.06
2 year	92.9	0.05	86	0.06
3 to 10 year	82.0	0.07	-	-

Table 10: showing post TIPS survival rates in two groups

Post TIPS survival rate in Gore Viatorr at 3month to 1 year, 2 years and at 3 to 10 years was 97.9%, 92.9%, 82% respectively.

Post TIPS survival rate in Niti-S at 3month to 1 year, 2 years and at 3 to 10 years was 86%.

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	2.474	1	.116
Tarone-Ware	2.547	1	.110

Table 11: comparision of post TIPS survival rate among two groups

P value is not less than 0.005, hence there is no significant difference between the post op survival rate of Gore Viatorr and Niti-S patients.

Liver transplant:

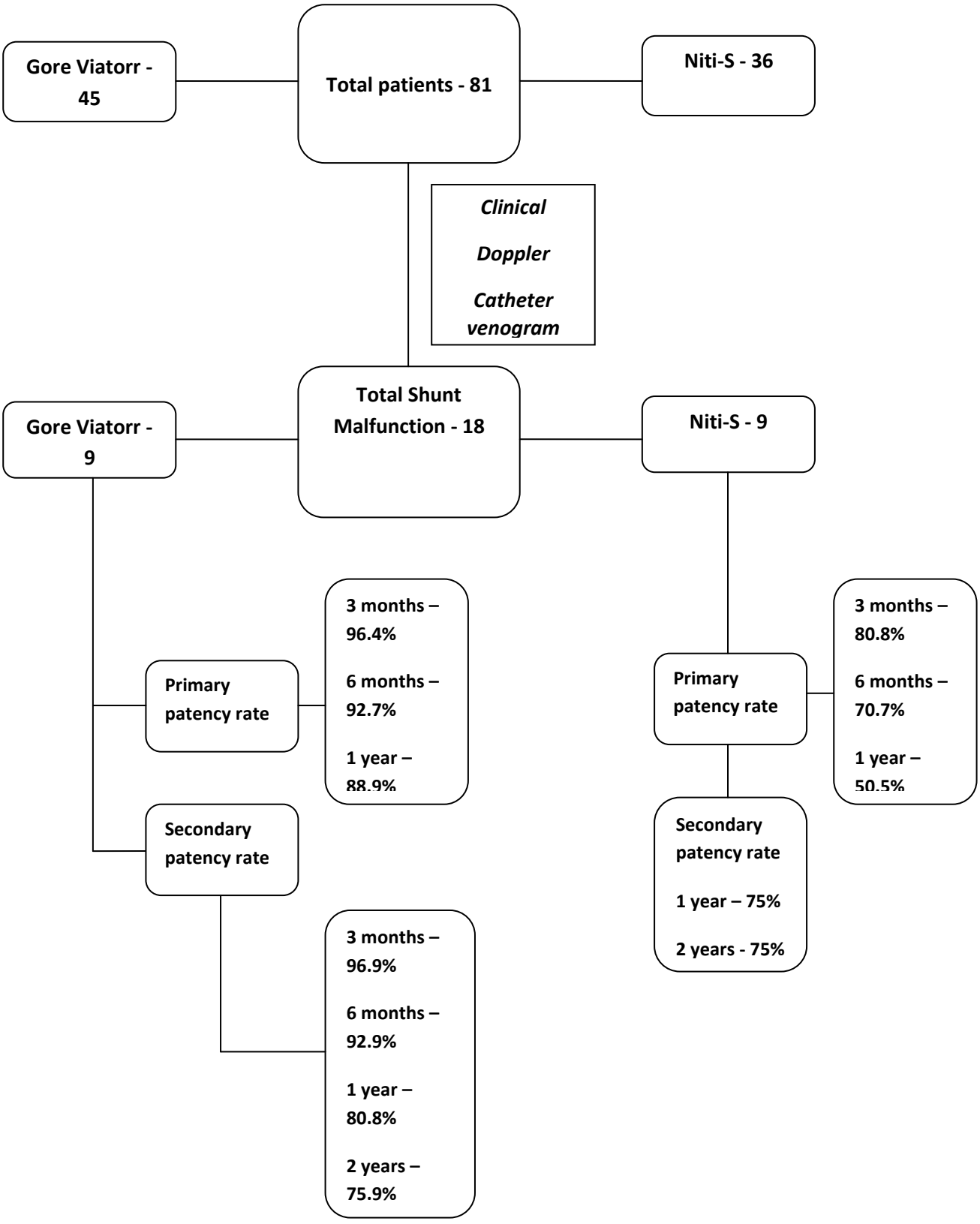
3 patients underwent liver transplant within 1-3 months post TIPS. Out of 3, 1 of them had Gore Viatorr stent and 2 had Niti-S stent placement.

Additional stent placement:

Total 6 patients had additional stent placement. 3 of them were placed along with the main stent itself during the TIPS procedure. All these additional stents placed were Fluency stents and all the patients had Gore Viatorr as the main stent.

3 patients had an additional stent placement within the previous stent as part of treatment. In these patients when the shunt stenosis was not relieved even after balloon angioplasty they had additional stent placement within the previously existing stent. One patient belonged to Gorre Viatorr and other 2 belonged to Niti-S group of patients.

SUMMARY OF RESULTS:



DISCUSSION:

TIPS is a well established technique worldwide to treat portal hypertension complications. Image guided parenchymal shunt is created between systemic and portal circulation to decrease the portal pressure.

If the shunt is created between the hepatic vein and portal vein it is called as TIPS, most commonly right hepatic vein is used.

If the shunt is created between the IVC and portal vein it is called as DIPS.

Main complication of the procedure is shunt malfunction which can be due to shunt occlusion or shunt stenosis (28). In the initial days with the use of bare metal stents shunt failure rate was much higher. With the introduction of covered stents shunt patency has significantly improved (28).Which in turn has increased the symptom free period, has reduced the need of multiple shunt revisions and has reduced the mortality.

Various stent grafts materials are recommended, of which e-PTFE lined Gore Viatorr stent is most commonly used stent. This e-PTFE covering helps in preventing passage of bile in to the stent and also prevents instent parenchymal protrusion. Both these make the stent highly non thrombogenic (28). Various studies were done to compare patency rate of Gore Viatorr and bare metal stents. Over a time Gore Viatorr has emerged as a stent with much better patency rate. A large multicenter study was done in Italy for 113 patients which showed primary patency rate of Gore Viatorr to be 92% at 6 months, 80% at 1 year and 76% at 2 years (2).

Gore Viatorr was introduced in 1999, after European multicenter trial, available since 2001, FDA approval in December 2004 (24). In India it is available since 2005. Gore Viatorr stent is not available in India since 2015, hence in our department Niti-S stent is been used instead till date. English literature available about Niti-S TIPS stent patency and clinical outcome are sparse and furthermore no Indian study is available.

Hence comparision between Gore Viatorr and Niti-S stents was done in terms of clinical outcome, primary and secondary patency rates.

In our study total 81 patients with stent grafts were analysed. 45 patients had Gore Viatorr and 36 patients had Niti-S stent placement. In all the patients with Gore Viatorr stent TIPS procedure was done before 2015, hence all this data was retrospectively analysed. Patients with Niti-S stent placement form July 2016 to August 2017 underwent prospective analysis.

Variables studied were age, sex, pre and post TIPS pressure, clinical outcome, Doppler findings, catheter venogram findings, number of shunt revisions needed and death of the patients.

Post TIPS these patients had a regular follow up at 1 week, 1 month, 3 month, 6 month, 1 year and every 1 year thereafter. Regular follow up included clinical and Doppler examination. Shunt patency was determined by combining clinical findings, Doppler findings and catheter venogram findings.

Shunt malfunction was either due to shunt occlusion or shunt stenosis. Those patients who had shunt stenosis were treated with balloon angioplasty.

Those patients with shunt occlusion were treated with thrombolysis/ thrombectomy and balloon angioplasty.

Mean follow time for Gore Viatorr patients was 7 years +/- 1 year and for Niti-S patients was 1.1 years +/- 2 months.

Patency rates were determined using survival analysis (Kaplan Meier curves).Primary patency rate of Gore Viatorr stent at 3 month, 6 month, 9 month, 1 year and 2 years were 96.4%, 92.7%, 88.9%, 88.9%, 76.7% respectively.

Primary patency rate of Niti-S stent at 3 month, 6 month, 9 month, 1 year and 2 years were 80.8%, 70.7%, 70.7%, 50.5%, 37.9% respectively. Association between patency rates was calculated using chi square test which showed that there is significant difference between these two groups.

Secondary patency rates of Gore-Viatorr at 3 month, 6 month, 9 month, 1 year and 2 years were 96.9 %, 92.9%, 89%, 85%, 75.9% respectively. Secondary patency rate of Niti-S at 1and 2 years was 75%. But statistical analysis did not show any significant difference between the secondary patency rate of both stents.

Post TIPS survival rate in Gore Viatorr at 3month to 1 year, 2 years and at 3 to 10 years was 97.9%, 92.9%, 82% respectively. Post TIPS survival rate in Niti-S at 3month to 1 year, 2 years and at 3 to 10 years was 86%.Statistically there was no significant difference between the two groups

Comparison with other studies:

Comparisons of patency rates of Gore-Viatorr was made with an Italian study published in August 2005(28).

Time	Primary patency rate (%) **Our study** (n=45)	Primary patency rate (%) **Italian study** (n=113)
3 months	96.4%	-
6 months	92.7%	91.9%
1 year	88.9%, %	79.9%
2 years	76.7%	75.9%

Table 12: comparing primary patency rates for Gore Viatorr stent in our study and Italian study

Italian study had a sample size of 113 as against 45 for Gore Viatorr patients in our study. Most common cause of portal hypertension was viral hepatitis with 58 patients accounting for 51% of cases in Italian study whereas in our study it was Budd Chiari syndrome with 33 patients accounting for 73% of cases. Italian study had only 2 patients with Budd Chiari syndrome. In Italian study most common indication of TIPS was refractory ascites followed by variceal bleeding with 52 and 49 cases each

accounting for 45% and 43%. In our study most common cause of indication was refractory ascites accounting for 80% of cases.

In the reference study 3 month primary patency rate was not calculated, 6 month and 2 year primary patency rates were similar to our study. 1 year primary patency rate in our study was better (88.9%) compared to the reference study (79.9%) the cause for which is not obvious. Secondary patency rate was 98.2%, but the time interval was not described, hence exact comparison of the secondary patency rates could not be done.

Comparison of primary patency rates for Niti-S stent were made with Korean study published in March 2002(25) and Italian study done in June 2004 (30).

Time	Primary patency rate (%) **Our study**	Primary patency rate (%) **Korean study (March 2002)**	Primary patency rate (%) **Italian study (June 2004)**
3 months	80.8%	-	-
6 months	70.7%	77%	-
1 year	50.5%	72%	83.8%

Table 13: comparing primary patency rates for Niti-S stent in our study, Korean and Italian study

Time	Secondary patency rate (%) **Our study**	Secondary patency rate (%) **Korean study (March 2002)**	Secondary patency rate (%) **Italian study (June 2004)**
1 year	-	-	98%
2 year	75%	95.4%	---

In Korean study with sample size of 22, most common cause of indication for TIPS was variceal bleeding. In our study with sample size of 37 for Niti-S group of patients, most common cause of indication for TIPS was refractory ascites. In Korean study most common cause for portal hypertension was viral hepatitis accounting for 18 patients followed by alcoholic liver disease accounting for patients, this study did not have any patient with Budd Chiari syndrome syndrome. In our study most common cause for portal hypertension was Budd Chiari syndrome syndrome, 23 patients had Budd Chiari syndrome syndrome, 7 patients had alcoholic liver disease and only 3 had viral hepatitis as against 18 patients in Korean study. In Korean study primary patency rates at 3 months was not calculated. Compared to this study, our study showed lower primary patency rates at 6 months and 1 year and lower secondary patency rate at 2 years.

Italian study had sample size of 53 which was larger than our study. Most common cause of indications for TIPS and cause of portal hypertension were variceal bleeding and viral hepatitis respectively as against our study, but was similar to the above Korean study. Italian study had only 2 patients of Budd Chiari syndrome accounting for only 3.7% of patients as against our study where Budd Chiari syndrome accounted for 63.8 of patients.

Primary patency rate and secondary patency rate at only 1 year was calculated. In comparision our study showed lower patency rates.

Most common cause of portal hypertension in our study was Budd Chiari syndrome . Out of total 81 patients 56 had Budd Chiari syndrome accounting for 69% of cases. Out of total 18 patients who had shunt malfunction, 16 had Budd Chiari syndrome as a cause of portal hypertension, 1 had alcoholic liver disease and 1 had cryptogenic fibrosis. Out of total 18 patients, 4 were diagnosed to have hypercoagulable state. Out of this remaining 14 patients 12 had Budd Chiari syndrome and 2 had other causes. As Budd Chiari syndrome can result due to underlying hypercoagulable state, which can be possibly one of the cause for higher shunt malfunction and lower patency rates in our study.

LIMITATIONS:

1) Sample size as calculated could not be achieved due to the time availability. Further recruitment of this study is ongoing.
2) Many patients were lost to follow up which is an obvious limitation of the study.
3) All the patients who had shunt block were not evaluated for hypercoagulable state which can be possibly one of the cause of lower patency rates in Niti-S group in our study.
4) Additional Fluency stent was placed in patients who had Gore-Viatorr in 3 patients of this 1 patient had shunt malfunction at 4 year post TIPS, this is was not analysed separately.

CONCLUSIONS:

1) Primary patency rate of Gore-Viatorr at 3 months is 94.6 % and that of Niti-S is 80.8%.
2) Secondary patency rate of Gore Viatorr at 24 months is 76% and that of Niti-S is 75%.
3) Overall clinical outcome and primary patency rate of Gorre Viatorr stent is better than Niti-S stent.
4) Secondary patency rates of Gore Viatorr and Niti-S at 24 months are similar.

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ANNEXURES:

Annexure 1a: Information sheet and consent form in English

Department of Radiodiagnosis, Christian Medical College, Vellore

Study Title: Comparison of efficacy of different stents used for TIPS procedure

INFORMATION SHEET PATIENT

You are being requested to participate in a study to compare the clinical outcome and patency rates of different types of stents used in TIPS procedure. Only a particular type of stent called Niti-S stent is used in Department of Radiology, CMC Vellore since last year due to non availability of Viatorr Gore stent in India. At the end of study we may be able to tell which stent has the best clinical outcome and patency rate. Also we may be able to provide better information about clinical outcome and patency rate of Niti-S stent as very less information is available about this stent.

What additional tests do I have to go through if I take part in this study?

If you take part in this study, you will have to come for regular follow up in OPD and also undergo frequent Doppler scans as prescribed by your clinician. You will not have to pay any additional amount.

Does Doppler have any side effects?

Doppler does not have any harmful radiation. We will be doing it the same way as you would have it if you were not included in this study but more frequently

If I take part in this study, what will I have to do?

If you agree to participate in this study, there will be no change in the other investigations and treatment that you will be receiving. You will be expected to come to the OPD and for the Doppler scan as advised by your doctor. No additional blood tests will be done as a part of this study.

Can I withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if I develop any study related injury?

This scan does not involve harmful radiation and it is non- invasive. So, we do not expect any major procedure related injury. However you can immediately report to us.

Will I have to pay for the additional tests?

Doppler scan is usually done as a part of your routine tests. You will not have to pay any additional amount than that is required. All other investigations, as requested by your doctor will continue in the usual manner. How much you pay for these investigations will not change and this has nothing to do with your participation in this study.

What happens after the study is over?

You will benefit from this study as you will be regularly followed up, any problem will be identified early and necessary treatment will started. Once the study is over, we will analyze the results and come to a conclusion and we will be able to use these results and find out which stent has the best clinical outcome and patency rate. Also we may be able to provide better information about clinical outcome and patency rate of Niti-S stent as very less information is available about this stent.

Will my personal details be kept confidential?

The results of this study will/may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical record may be reviewed by doctors associated with the study, without your additional permission.

If you have any further questions, please contact Dr. Manisha Mane (Tel: 0416 228-3012/2027/3609) between 8am & 4:30pm from Monday to Friday and from 8am to 12:30pm on Saturday or you can email your queries to drmanemanisha@gmail.com .

Department of Radiodiagnosis, Christian Medical College, Vellore

CONSENT TO TAKE PART IN TIPS RELATED STUDY

Study Title: Study Title: Comparison of efficacy of different stents used for TIPS procedure

Serial Number:
Patient's name:
Hospital No:
Date of Birth / Age (in years):
(Please tick boxes)
(i) I _____declare that I have read / been read to the information sheet provided to me regarding this study and have clarified any doubts that I had. [ ]

(ii) I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting patient's usual treatment or legal rights [ ]

(iii) I understand that study staff and institutional ethics committee will not need my permission to look at patient's health records if I withdraw from the trial. I agree to this access [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose[ ]

(v) I understand that patient's identity will not be revealed in any information released to third parties or published [ ]

(vi) I voluntarily agree to take part in this study [ ]

Name :

Signature/ Thumb Impression

Date:

Name of witness

Signature / Thumb impression

Date

Annexure 2: Proforma for data collection

Department of Radiodiagnosis, Christian Medical College, Vellore

COMPARISION STUDY OF DIFFERENT STENTS USED FOR TIPS

1. Serial number:

2. Name of patient:

3. Age/ Sex:

4. Hospital number:

PROFORMA

5. Date of TIPS procedure:

6. Indication for TIPS:

i. Refractory ascites

ii. Refractory hydrothorax iii. Variceal bleeding

iv. Bridge to Liver transplant

7. Cause of portal hypertension:

i. Budd Chiari syndrome ii. Alcohol

iii. HBV/HCV

iv. Others (NAFLD, Cryptogenic, non cirrhotic portal hypertension)

8. Type of stent used:

i. Gore Viatorr

ii. Niti-S:

9. Length and diameter of the stent:

10. Post procedure follow up to one week: I. Symptoms: a) no new symptoms b) worsening of symptoms II. Doppler: a) patent b) block c) Velocity within shunt: at portal end-----, mid stent----, caval end---- i. between 90-190 cm/sec (normal) ii. below 90 cm/sec (abnormal) iii. above 190 cm/sec (abnormal)

I. Symptoms: a) no new symptoms b) worsening of symptoms

II. Doppler: a) patent b) Thrombosed

c) Velocity: at portal end-----, mid stent----, caval end---- i. between 90-190 cm/sec

ii. below 90 cm/sec

iii. above 190 cm/sec

III. If stent thrombosis: Treatment details like thrombolysis, balloon plasty or another stent placement

11. Follow up at 1-2months:

I. Symptoms: a) no new symptoms b) worsening of symptoms

II. Doppler: a) patent b) block

c) Velocity within shunt: at portal end-----, mid stent----, caval end----

i. between 90-190 cm/sec (normal)

ii. below 90 cm/sec (abnormal)

iii. above 190 cm/sec (abnormal)

d) Velocity within main portal vein:

i. Above 30cm/sec (normal)

ii. below 30cm/sec (abnormal) III. Catheter venogram: a) Normal b) Stenosis c) Occluded

IV. Balloon angioplasty: a) done b) Not required

V. New stent placed: Yes /No

12. Follow up at 3-4 months: I. Symptoms: a) no new symptoms b) worsening of symptoms II. Doppler: a) patent b) block c) Velocity within shunt: at portal end-----, mid stent----, caval end---- i. between 90-190 cm/sec (normal) ii. below 90 cm/sec (abnormal) iii. above 190 cm/sec (abnormal) d) Velocity within main portal vein: i. Above 30cm/sec (normal) ii. below 30cm/sec (abnormal) III. Catheter venogram: a)

Normal b) Stenosis c) Block IV. Balloon angioplasty: a) done b) Not required V. New stent placed: Yes /No

13. Follow up at 6-7 months:

I. Symptoms: a) no new symptoms b) worsening of symptoms

II. Doppler: a) patent b) block

c) Velocity within shunt: at portal end-----, mid stent----, caval end----

i. between 90-190 cm/sec (normal)

ii. below 90 cm/sec (abnormal)

iii. above 190 cm/sec (abnormal)

d) Velocity within main portal vein:

i. Above 30cm/sec (normal)

ii. below 30cm/sec (abnormal) III. Catheter venogram: a) Normal b) Stenosis c) Block

IV. Balloon angioplasty: a) done b) Not required

V. New stent placed: Yes /No

14. Follow up at 12-13 months: d) Velocity within main portal vein: i. Above 30cm/sec (normal) ii. below 30cm/sec (abnormal) III. Catheter venogram: a) Normal b) Stenosis c) Block IV. Balloon angioplasty: a) done b) Not required V. New stent placed: Yes /No

15. Follow up at One and half year :

I. Symptoms: a) no new symptoms b) worsening of symptoms

II. Doppler: a) patent b) block

c) Velocity within shunt: at portal end-----, mid stent----, caval end----

i. between 90-190 cm/sec (normal)

ii. below 90 cm/sec (abnormal)

iii. above 190 cm/sec (abnormal)

d) Velocity within main portal vein:

i. Above 30cm/sec (normal)

ii. below 30cm/sec (abnormal) III. Catheter venogram: a) Normal b) Stenosis c) Block

IV. Balloon angioplasty: a) done b) Not required

V. New stent placed: Yes /No

16. Follow up at 2 years :

I. Symptoms: a) no new symptoms b) worsening of symptoms

II. Doppler: a) patent b) block

c) Velocity within shunt: at portal end-----, mid stent----, caval end----

i. between 90-190 cm/sec (normal)

ii. below 90 cm/sec (abnormal)

iii. above 190 cm/sec (abnormal)

d) Velocity within main portal vein:

i. Above 30cm/sec (normal)

ii. below 30cm/sec (abnormal) III. Catheter venogram: a) Normal b) Stenosis c) Block

IV. Balloon angioplasty: a) done b) Not required

V. New stent placed: Yes /No

17. Balloon angioplasty done or not

I. Yes

II. No

If yes follow after balloon angioplasty:

I. Symptoms: a) no new symptoms b) worsening of symptoms

II. Doppler: a) patent b) block

c) Velocity within shunt: at portal end-----, mid stent----, caval end----

i. between 90-190 cm/sec (normal)

ii. below 90 cm/sec (abnormal)

iii. above 190 cm/sec (abnormal)

d) velocity within main portal vein:

i. Above 30cm/sec (normal)

ii. below 30cm/sec (abnormal) III. Catheter venogram: a) Normal b) Stenosis c) Occluded

IV. Balloon angioplasty: a) done b) Not required

18. Lost to follow up

19. Death of patient: Yes/NO If yes: cause of death

Annexure 3: IRB protocol

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 1

APPLICATION FOR IRB APPROVAL OF OBSERVATIONAL

(CASE-CONTROL / COHORT/ CROSS-SECTIONAL) STUDIES

CHRISTIANMEDICALCOLLEGE, VELLORE

(Please complete Sections **I to III** and submit with all supporting documents)

SECTION I

Fluid Research Funding/External Funding (delete as appropriate)

If for external funding, please provide name of funding agency and the application

for submission in the funding agency's format, in addition to this application.

1. Title of Research: Comparison of clinical outcome and patency of Gore-Viatorr and Niti-S stents

used in Transjugular intrahepatic portosystemic shunt (TIPS)

2. Title of Study(for lay public): A study to evaluate which is the best stent for Transjugular

intrahepatic portosystemic shunt procedure

3. Acronym if any: Nil

4. Unique Protocol ID, if any: Nil

5. **Name of the Principal Investigator:** Dr. Manisha Sheshrao Mane

Designation / Department / Unit / of Principal Investigator: 1st year PG, Radiology

Department

Employment Number: 33298

Address for communication (including telephone and fax numbers and email id):

2D4-House no 60, CMC Nursing college campus, Kagithepetterai, Vellore 632004

Mobile number: 9655992163

If Post Graduate Registrar: Yes

Enrollment date of PG Course: 01/04/2015

Completion date of PG Course: 30/03/2018

6. Name of Guide (for Post-Graduate Registrar / Fellowship):

Dr. Munawwar Ahmed

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 2

Associate Proffesor,

Christian medical college, Vellore,

Employment Number: 32015

Address for communication (including telephone and fax numbers and email id):

Telephone: 0416307 3012/ 3609

Email id: munawwarahmed19@yahoo.co.in

7. Name and Designation of Co-Investigator(s), Employment Number and Address :

Dr. Shyamkumar N. Keshava

Professor and Head,

Department of Radiology,

Christian Medical College Hospital,

Ida Scudder road,

Vellore

India. 632004

aparna_shyam@yahoo.com

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Dr. Vinu Moses

Professor,

Department of Radiology,

Christian Medical College,

Vellore, Tamil Nadu.

Employment number: 28371

Email id: vinu@cmcvellore.ac.in

Dr. George Koshy Chiramel

Associate professor,

Department of Radiology,

Christian Medical College Hospital,

Ida Scudder road

Vellore

India. 632004

Dr. C.E.Eapen

Professor and Head of Clinical Gastroenterology and Hepatology,

Christian Medical College,

Vellore, Tamil Nadu.

Email id: eapen@cmcvellore.ac.in

Contact number: 2496 / 2148

Dr. Uday George Zachariah,

Title of Research Project:

Professor and Acting Head of Hepatology,

Christian Medical College,

Vellore, Tamil Nadu.

Email id: udayzachariah@cmcvellore.ac.in

Contact number: 2496 / 2148

Dr. Ashish Goel

Professor of Hepatology,

Christian Medical College,

Vellore, Tamil Nadu.

EMP no. 31642

Email id: drashishgoel@cmcvellore.ac.in

Contact number: 2496 / 2148

8. Department of Institution where the research will be carried out: Department of Radiodiagnosis,

CMC Vellore, 632004

9. **Names and addresses of other institutions where research will be carried out:** Nil

10. Duration of the Scheme: 13-14 months

11.**Source/s of Monetary or Material Support**

Internal - Fluid /Major Research Grant: Yes

External : Nil

Departmental fund : Nil

12.**Permission letter from the HOU & HOD of each unit/department involved in the study. If Medical students, Nursing students & Allied Health students, nurses, are involved in the study a permission letter from the appointing authority has to be enclosed:** Not applicable

13. **If this is a laboratory study if you have out sourced genetic test to be an external laboratory. Please provide evidence of the laboratory credentials.**

Not applicable

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 4

14. Is this an invention or idea that you plan to register as a

patient: No

15. Objectives and aims of study (*including any hypotheses).*

® To compare primary patency at 3 months and secondary patency rates at 24 months of Viator

Gorre and Niti-S stents

® Which stent has the best primary patency rate?

® To compare clinical outcome of Gore-Viatorr and Niti-S stents

16. Summary of the proposed research scheme (250 words).

In the Department of Radiology, CMC Vellore various stents such as Uncovered,

Gore Viatorr, Uncovered-Covered and Niti-S TIPS stents have been used. In the year of

2015 only Niti-S TIPS stent was used due to non-availability of Gore Viatorr stent in

India.

® In this study comparison of clinical outcome and primary and secondary

patency of Gore-Viatorr and Niti-S stents will be conducted. All the patients who

have undergone TIPS procedure in Department of Radiology and patients

undergoing TIPS for next 1 and half years will be included in this study.

Data from the year of 1999 will be collected and retrospectively analyzed, whereas

Data collected from patients undergoing TIPS for next 1 and half years will be

prospectively analyzed.

17. Present Knowledge and relevant bibliography *(Is there a justification for this study based*

on a detailed literature review or other sources of evidence? Please provide details)

Title of Research Project:

Transjugular intrahepatic portosystemic shunt (TIPS) has played an important role in managing and treating complications of portal hypertension like variceal bleeding and refractory ascites/hydrothorax. In the early years, mortality and shunt patency due to shunt dysfunction was high due to use of bare metal stents. Long term shunt patency was significantly improved following introduction of covered stent (1). Amongst the various covered stents used, Gore Viatorr stent is most commonly used stent.

Various stents used in Department of Radiology, CMC Vellore are

-Gore Viatorr stent

-Uncovered

-Covered-Uncovered

- Niti-S TIPS stent

Gore Viatorr stent:

-Introduced in 1999, after European multicenter trial, available since 2001, FDA approval in

December 2004 (2)

-In India available since 2005

-Structural support is provided by an external self-expanding nitinol stent (4)

-Intrahepatic portion of the stent is covered with PTFE whereas the bare part lies in the portal

vein (3)

-Covered and uncovered portion, interface is demarcated by radio-opaque gold ring(4)

-Additional radiopaque gold marker is at the proximal end which helps fluoroscopic visualisation

during deployment (3)

Angermayr et alhave retrospectively demonstrated an improved survival rate of 88% at 1 year for

patients treated with theVIATORR1 endoprosthesis for TIPS, compared with 73% for a matched

group receiving bare stents. Survival rate after TIPS creation with the VIATORR device is higher

than that after TIPS creation with an uncovered stent (3)

Niti-S TIPS stent:

-This stent has been used exclusively in our departmentsince 2015 onwards as Gore Viatorr is

not available in India

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 6

-Niti-S TIPS stent is being used since 2015 onwards as Gore Viatorr is not available in India

English literature available about Niti-S TIPS stent patency and clinical outcome are sparse and

furthermore no Indian study is available.

-It is a mesh-type stent interlaced with a nitinol monofilament. (4)

-Nitinol monofilament wire is wound on a mandrel to create a spiral mesh at deployment, the

stent self-expands to a predetermined diameter of 8–10 mm with a length of 6–10 cm.(4)

-It has constant 20mm uncovered portion and variable covered portion [varying from 40mm to

100mm (4)

Following are few overseas studies conducted for Niti-S TIPS stent which suggests that primary

patency of this stent is lesser than that of Gore Viatorr stent:

A New Nitinol Monofilament Stent (Niti-S stent): Early Experience with Use for Transjugular

Intrahepatic Portosystemic Shunts, Cardiovascular and Interventional Radiology, 27 March 2002

(5)

Sample size 22

Primary patency rate 77% at 6 months

72 % at 1 year

Secondary patency rate 95 % up to 26 months

Rossi P, Bezzi M, Salvatori FM, et al. (1996) Self-expanding (uncovered)stents in Transjugular

intrahepatic portosystemic shunt: Experience with nitinol Strecker stents(Niti-S stents),

Rome,EUR radiology 6:741–747 (6)

Sample size 48

Primary patency rate 25 to 66% at 6 months

Secondary patency rate 80-89 % at 6-24 months

Doppler evaluation: (7)

Normal Values:

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 7

Shunt velocity: >90 cm/sec or <190 cm/sec

MPV velocity: should be more than 30 cm/sec

Shunt malfunction-Doppler evaluation: (7)

® Due to narrowing or occlusion - intimal hyperplasia or insitu thrombosis

® Most common site for occlusion or stenosis is cephalic portion/portal end

® Occlusion - absent flow at colour Doppler

® Stenosis - abnormally high (>190 cm/sec) / abnormally low (<90 cm/sec) velocity within

the shunt or increase or decrease >50 cm/sec compared with the prior examination

® Portal venous flow changes from hepatofugal to hepatopetal flow

® MPV-Low velocity (<30 cm/sec)

® Development or recurrence of collateral vessels such as a recanalized umbilical vein

® New, recurrent, or worsening ascites

References:

1.Clinical outcomes of Transjugular intrahepatic portosystemic shunt for portal hypertension:

Korean multicentrereal-practice data,

Hyung Ki Kim1,Dae Won Jun8, Moon Young Kim13, Soo Young Park14, Jae Myeong Lee15,

and Young Seok Kim1, Yoon Jun Kim2, Soon Ho Um9, Woo Jin Chung3, Sung Jae Park10,

Young Woo11, Young Kul Jung12, Soon Koo Baik13, Soon Sun Kim4, Jae Jun Shim5

Department of Internal Medicine, Soonchunhyang University College of Medicine, Bucheon; 2

Research Institute, Article in clinical and molecular hepatology, 2014

2. Should Stent-Grafts Replace Bare Stents for Primary TransjugularIntrahepatic

Portosystemic Shunts?

Manfred CM.D.,1Section of Interventional Radiology, Vienna Medical School, Austria; and

Department of Radiology, LKH Feldkirch, Feldkirch, Austria

Seminar Intervention Radiology, 2005 Dec; 22(4): 287–299.

3. Transjugular Intrahepatic Portosystemic Shunts: An Update;

Title of Research Project:

Editors in Chief, Brian Funaki, M.D., Peter R. Mueller, M.D.; Guest Editor, Hector Ferral, M.D.

Seminars in Interventional Radiology, volume 22, number 4, 2005.

4. A New Nitinol Monofilament Stent: Early Experience with Use for Transjugular

Intrahepatic Portosystemic Shunts,

Chang Ji ,Radiologyn Yoon, Jin oo ChuHyun, KiJoWoo Lee, Jae Hyung Park,

CardioVascular and Interventional Radiology, 27th march 2002

5. A new Nitinol Monofilament Stent (Niti-S stent): Early Experience with Use for Transjugular

Intrahepatic Portosystemic Shunts,

Chang Jin Yoon, Jin Wook Chung, Hyun Beom Kim, Joon Woo Lee, Jae Hyung Park

Department of Radiology and the Institute of Radiation Medicine, Seoul National University

College of Medicine, 28 Yongon-Dong,

Cardiovasc Intervent Radiol (2002) 25:200–204

Published on 27 March 2002

6. Self-expanding stents in transjugular intrahepatic portosystemic shunt: Experience with

nitinol Strecker stents

Rossi P1, Bezzi M, Salvatori FM, Broglia L, Maccioni F, Pizzi G, Abbondanza S, Bonomo

G.

Department of Radiology, University of Rome La Sapienza, Policlinico Umberto I, Italy.

EUR radiol 1996;6(5):741–7

7. Doppler US of the Liver Made Simple, Gastrointestinal imaging,

Dean Alexander McNaughton, MD, and Monzer M. Abu-Yousef, MD,

RSNA, Radiographics, January-February 2011, Volume 31, Issue 1

18. Preliminary work already done by the investigator in this problem :

- Retrospective pilot study was done for a period of 3 years from 2013 to 2015 for 45 patients.

- Gore Viatorr, Uncovered, Covered-uncovered, Niti-S TIPS stents were used in these patients for TIPS procedure.

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 9

This retrospective pilot study showed that Primary patency rate of Niti-S TIPS stent at the end of one month is less compared to other stents.

However the secondary patency rate appeared similar to Gore Viatorr Stent

19. List of publications of the investigator in the field: Nil

Retrospective pilot study, 3 years

(2013-2015)-45 patients

Gore Viatorr-14

Covered--uncovered-12

Uncovered-3

Niti-S-14

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 10

20. Structured abstract (Structured abstract should be in future tense)

® Aim: To compare the clinical outcome and patency rates of Gore-Viatorr and Niti-S stents

used in Transjugular intrahepatic portosystemic shunt (TIPS)

® Methods: All the patients who have undergone TIPS procedure in the Department of

Radiology, CMC Vellore from 1999 onwards will be included in the study

-All patients coming to CMC who have already undergone TIPS procedure will be

retrospectively analyzed

- Patients who will need TIPS will undergo prospective analysis. In these patients NITI S

stents will be used unless Gore Viator stent becomes available

® Results:

Clinical outcome and patency rates of two different stents used for TIPS procedure will be

compared, Primary patency rate will be calculated at the end of 1 year

We aim to determine the patency rate of the Niti-S TIPS stent, and whether it has a

better or equivalent patency rate compared to Gore-Viatorr stent

21. Detailed diagrammatic Algorithm of the study:

Patient

Clinical assessment in OPD

Doppler / CT (Radiology)

Procedure (TIPS/DIPS)

Follow up

Post procedure follow up to 1 week; 1, 3, 6 months 1st year,

every 6 monthly after 1 year

Asymptomatic &normal Doppler Symptomatic & normal Doppler Asymptomatic &abnormal Doppler Symptomatic &abnormal Doppler

Follow up Follow up

Catheter venogram

Normal Abnormal

Title of Research Project:

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22. Detailed research plan:

a. **Setting:** Describe the setting, locations, and relevant dates, including periods of

recruitment, exposure, follow-up, and data collection

Patients who have already undergone TIPS procedure from 1999 onwards in the Department of Radiology, CMC Vellore will be included in the study.

Patients who will undergo TIPS procedure for next 13-14 months will also be included in the study.

Data collected from 1999 onwards will be retrospectively analysed

Data collected from patients undergoing TIPS procedure with Niti-S stent for next 13-14 months will be prospectively analysed

Participants: Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases (and controls, if applicable). For matched studies, give matching criteria and the number of controls per case

Patients who have already undergone TIPS procedure from 1999 onwards will be included in the study and retrospectively analysed.

Patients who will undergo TIPS procedure for next 13-14 months will also be included in the study and will undergo prospective analysis.

b. **Variables:** Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable

Efficacy of various stents will be analysed based on following parameters:

Outcome will be measured in the form of Clinical outcome, Doppler and Catheter venogram

findings, Shunt blockage, number of shunt revisions required and death of the patient

Potential confounders are age, severity of cirrhosis of liver and cause of cirrhosis of liver as patients with Budd Chiari tend to be younger and patients with alcoholic liver disease and cirrhosis secondary to HBV/HCV infection tend to be older and

have more severe cirrhosis of liver

There are no effect modifiers in this study

Follow up Balloon angioplasty

Follow up

Title of Research Project:

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c. **Data Sources/measurement:** For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

1. Clinical outcome will be analysed in terms of whether there is decrease in symptoms, onset of new symptoms or worsening of symptoms.

2. Doppler evaluation of the shunt, whether it is patent or blocked, velocities within the shunt and main portal vein.

Shunt velocities will be taken at portal end, mid shunt and caval end. Velocities should be within 90-190 cm/sec range. Velocity above below 90 and above 190 will be considered abnormal.

Main portal vein velocity should be above 30 cm/sec, velocities below 30cm/sec will be considered abnormal.

Doppler evaluation will be part of a routine procedure

3. Catheter venogram: If the patient is symptomatic and Doppler is abnormal patient will be

called for follow up

If patient is symptomatic and Doppler is abnormal or if patient is asymptomatic and Doppler is abnormal patient will undergo Catheter venogram

4. Balloon angioplasty: If Catheter venogram findings are abnormal patient will undergo

balloon angioplasty and then will be followed up

d. **Bias:** Bias may arise due to loss of follow up of patients and may affect analysis. Many of the patients who will undergo retrospective analysis have not followed up in CMC, we will maximize the input by calling them and reviewing their outside reports and scans

e. Sample size:(It may be suitable to have a statistician as a co-investigator)

The required sample size to compare the primary patency rates across Viator Gorre and Niti-S stents used in Transjugular intrahepatic portosystemic shunt (TIPS) was found to be 49 in each of the groups with 80% power and 5% level of significance when the expected difference in the patency rates was considered as 30%. However, the number of available Niti-stents are only 45 so far from the year 2000.

Also, we expect only about 25 – 30 cases more of Gore-Viatorr in the next 3 – 4 months. Hence this study will include all the available cases of Niti and Viator Gorre stents.

The above patency rates were obtained using the following references:

Title of Research Project:

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A New Nitinol Monofilament Stent (Niti-S stent): Early Experience with Use for Transjugular Intrahepatic Portosystemic Shunts, Cardiovascular and Interventional Radiology, 27 March 2002

Rossi P, Bezzi M, Salvatori FM, et al. (1996) Self-expanding (uncovered)stents in Transjugular intrahepatic portosystemic shunt: Experience with nitinol Strecker stents(Niti-S stents), Rome,EUR radiology 6:741–747 (6)

Formula:

Where, P1 = 77%

P2 = 50%;

Power = 80%; , Level of significance = 5%

Reference for the above formula: Sahai H, Kurshid A.

Formulae and tables for the determination of sample size and power in clinical trials for testing differences in proportions for the two sample design: a review. Statistics in Medicine, 1996; 15: 1-21.

Two Proportion - Hypothesis Testing - Large Proportion - Equal Allocation

Proportion in group (primary patency rate in Gore-Viatorr) 0.77 0.77 0.7 0.7 0.7 0.7

Proportion in group (primary patency rate in Niti S stents) 0.66 0.5 0.6 0.55 0.5 0.45

Estimated risk difference 0.11 0.27 0.1 0.15 0.2 0.25

Power (1- beta) % 80 80 80 80 80 80

Alpha error (%) 5 5 5 5 5 5

1 or 2 sided 2 2 2 2 2 2

Required sample size for each arm 263 49 35 6 93 60

Allocation

f. **Quantitative variables**: Explain how quantitative variables will be handled in the analyses. If applicable, describe which groupings were chosen and why

Age is the only continuous variable and it will be presented using mean with SD in both typed of stents. The age of the patients across the two stents will be compared using Independent t-test or Rank sum test whose choice will be based on the QQ plot.

g. **Statistical methods:** Describe all statistical methods, including those used to

control for confounding and examine subgroups and interactions. How will missing

data be handled? If applicable, how will matching of cases and controls be

handled? Describe any proposed sensitivity analyses.

-Primary patency rate and secondary patency rate will be presented as percentage (%) for

two groups.

-All Binary outcomes such as primary and secondary patency rates (symptoms, Doppler

findings, Catheter venogram findings) will be presented in both the stents as a frequency table and

percentages with 95% CI. They will also be shown and also by using bar plot.

-Comparison between the groups will be performed using Z test for 2 sample proportion

test.

-Association between patency rate and clinical outcome will be performed by using chi

square test. Logistic regression will also be used to find the association of patency rate

with clinical outcomes adjusting for confounders if any.

Title of Research Project:

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i. **Name & designation of the statistician involved in your project for Statistical**

Analyses:

Dr. Visalakshi Jeyaseelan

Emp. Number 31093

Dept. of Biostatistics, CMC, Vellore.

23.Complete budget plan

*For **FLUID research grant money cannot be allocated for travel of the investigators***

nor can job outsourcing *be covered with FLUID grants. Funding out of the institution*

can be given only for the special mission hospital grant

(From Fluid Research Fund, there are no grants for personnel except in a major grant

application, funding is limited ***Rs. 50,000/- per year*** *for two years for standard*

applications,

Rs. 2,00,000/- per year for two years for major applications*). Website link:*

http://172.16.11.136/Research/#. >Rules for Major Fluid Research Grants. Do not exceed

the budget allocated to you. In case the budget is exceeded, the amount will have to be

deducted from one of your departmental special funds. Stationary, printing material and

paper should not exceed more than 20% of the allocated fluid grant.

Please mention below the ***breakdown of budget requested:*** *(The budgets that are*

drawn up should becomprehensive and should mention all subject in detail (For example

– laboratory investigation should mention the specific category without generalization.)

Serial No ITEM Cost Number of

patients

Total

1. Doppler 2 x 2900 16 92,800

2. Stationary/ Printing/

Binding

6000 - 6000

Total Total = Rs.98,800/-

24. **Enclose proforma for Data collection*:***

Title of Research Project:

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Enclosed

25. If this is an application for Fluid Research Funding, please provide name and account number of any other Fluid Research grant held by the PI.

Fluid research grant applied

S. No Study Title IRB Min. No.

and date

Grant Sanctioned

amount/ Account Head

Duration /

Year

Study ongoing/

completed

26. Informed Consent Documents (patient information sheet, investigator's brochure,

drug information etc and informed consent document) please submit all translations with the

proposal**.**

Enclosed

We request waiver of consent for the retrospective group

Consent for the prospective group will be taken before the procedure

27. Publication Plans: (List all potential authors and their likely contributions)

(Please tick √ appropriate box)

Responsibilities

Author(s)

Name	Research and Study design	Data collection & analysis	Lab analysis	Interpretation and conclusion	Preparation of Manuscript	Review of Manuscript	Guide And critical revision	Administration	Technical Support
Dr. Manisha Mane	√	√	-	√	√	√	√	-	-

Dr.Munawwar Ahmed √ √ - √ √ √ √ - -

Dr.Shyamkumar N.

Keshava

√ √ - √ - √ √ - -

Dr. Vinu Moses √ √ - √ - √ √ - -

Dr. George Koshy

Chiramel

√ √ - √ - √ √ - -

Dr.C.E.Eapen √ √ - √ - √ √ - -

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 17

Dr.Uday George

Zachariah

√ - - √ - √ √ - -

Dr. Ashish Goel √ - - √ - √ √ - -

28. Inter-departmental cooperation: (Please describe the arrangements with institutional

diagnostic service units/departments that are being used for this research project, if applicable).

Patient will be clinically assessed in Hepatology OPD and DSA suite and will be sent to

Radiology Department for Doppler evaluation

29. Signature of Principal Investigator

30. Signature of Guide/Head of the Department/ Unit

31. Co-Investigators' Consent (all co-investigators have to sign this form or supply

separate letters of consent)

I/We give my/our consent to be a Co-Investigator and provide my/our expertise to the project.

I/We have approved this version of the protocol and have contributed substantially to its

development.

Name Department Signature Date

Dr. Munawwar Ahmed Radiology

Dr. Shyamkumar N. Keshava Radiology

Dr. Vinu Moses Radiology

Dr. George Koshy Chiramel Radiology

Dr. C.E.Eapen Clinical Gastroenterology

and Hepatology

Title of Research Project:

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Dr. Uday George Zachariah Hepatology

Dr. Ashish Goel Hepatology

Note: If the project is a resubmission a fresh copy of signatures needs to be obtained for

IRB

submission.

Section II

APPLICATION FOR APPROVAL FROM ETHICS COMMITTEE OF THE INSTITUTIONAL

REVIEW BOARD OF CMC VELLORE FOR ALL OBSERVATIONAL (CASE CONTROL,

COHORT & OBSERVATIONAL) STUDIES IN HUMAN SUBJECTS

1. Please provide a brief summary of the justification, objectives and methods in lay

language, avoiding technical terms:

Shunt is a track created between two vessels and stent is a mesh like metal pipe which is

placed within this track.

TIPS (Transjugular portosystemic shunt) is a procedure where a track is created between the

IVC/hepatic vein and portal vein which helps to reduce the portal pressure and tubular mesh

like metallic device is placed in this track which is called stent .

It is a useful treatment for patients suffering from symptoms of portal hypertension like fluid

accumulation in various parts of the body ie abdomen and chest, bleeding from mouth which

is not responding to the regularly used treatment

Different types of Stents are used for this procedure, In our study we want to find out whether

Gore Viatorr or Niti-S stent is better

Very less information is available about Niti-S stent, at the end of the study we will be able to

provide more information about Niti-S stent

2. Please describe if the study uses procedures already being performed on patients for

diagnosis or treatment or if modified or novel procedures are to be used?

Study uses procedures all being performed on patients

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 19

3. Please describe what benefits might be reasonably be expected by the participant as

an outcome of participation

-Only a particular type of stent called Niti-S TIPS stent is used in Department of Radiology,

CMC Vellore since last year due to non-availability of Gore Viatorr stent

-Very few overseas studies and no Indian study is available for Niti-S TIPS stent

-We aim to find out which type of stent doesn't get block early and hence reduces further

treatment required for this block and death rate

-We also want to find out whether Niti-S TIPS stent is better or same as commonly used

stents

-The participant may not get benefited directly from the study but results of study will be

helpful for providing exact information about the Niti-S TIPS stent

4. Please describe what benefits to others or new knowledge might be expected as a

result of this study

Results of study will be helpful for providing exact information about the Niti-S TIPS stent

5. Who are to be enrolled?

All patients who have undergone this procedure from 1999 onwards in department of

Radiology, CMC Vellore and also who will undergo the same procedure for 13-14

months from February 2016 to April 2017 will be included in the study

6. If any vulnerable groups (e.g., pregnant women, children) are to be enrolled, please

provide a justification for their inclusion.

Not involved

7. Mention how you will ensure that there is no undue inducement for participation of

economically disadvantaged persons among the likely participants in this study.

Participants of this study will not have to pay for the study. However the rest of the Investigations and treatment will be as decided by the treating clinician.

8. What are the potential risks to participants in this study?

There are no risks associated with this study**.**

9. Are the risks to participants reasonable in relation to the benefits that might reasonably be expected as an outcome to the participant or to others, or the importance of the knowledge that may reasonably be expected to result? Please provide a detailed description of the above.

Not applicable

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 20

10.Regarding informed consent to obtained from research participants or their legally

authorized representative(s):

a. **Does the informed consent document include all the required elements?**

Yes

b. **Are the participant information sheet and the consent document in language understandable to participants? (PLEASE PROVIDE WITH THIS SUBMISSION**

TRANSLATIONS IN ALL LOCAL LANGUAGES ANTICIPATED TO BE USED).

Yes

c. **Who will obtain informed consent (PI, nurse, other?) and in what setting?**

Primary investigator will obtain informed consent before performing the ARFI study**.**

d. **If appropriate, is there a children's assent? If yes, please submit a copy of this form.**

Not applicable

e. **Is the EC requested to waive or alter any informed consent requirement?**

No

11. Is there provision of free treatment for research related injury? If yes, who will

provide it?

There are no injuries related to the study

12. Is there provision for compensation of participants for disability or death resulting

from research related injury. If yes, who will provide it?

Not applicable

13. Is the study covered by insurance? If yes, please provide insurance documents from

an Indian insurance company.

No

14. In addition to the overall budget in Section I, please provide details of the following

i) Justification, timing and amount of payments to study participants

Not applicable

ii) **Justification,** timing and amount of payments to investigators/departments

Not applicable

iii) Any other study related financial or in kind incentives to participants or study staff

Not applicable

15. Please describe the plan for maintaining confidentiality of study participant

information.

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 21

All data obtained from a particular patient will have a unique identification code and the identity of the patient will not be revealed in any manner.

Patient's information and results of the study will not be accessible to anyone other than those involved in the study (staff)

16. Please describe the plans for monitoring the safety of participants, reporting and

managing adverse events. If this is an externally funded study with a Data Safety

Monitoring Board, please provide the name and contact information of the DSMB

chairperson.

Data will be stored in a password protected computer

Only the principal investigator/co investigators will have access to the

patient data.

Patient data will be stored in a password protected computer and data will be

deleted when no longer required**.**

17. If applicable; please provide all significant previous decisions (e.g., those leading to a

negative decision or modified protocol) by other ECs or regulatory authorities for the

proposed study (whether in the same location or elsewhere) and an indication of the

modification(s) to the protocol.

Not applicable

18.If appropriate, has permission from the Drug Controller General of India been

obtained?

Not applicable

19.If this is international collaborative research, has permission from the Health Ministry's Screening Committee been obtained?

Not applicable

20.For exchange of biological material in international collaborative studies, provide a Memorandum of Understanding (MOU)/ Material Transfer Agreement (MTA) between the collaborating partners.

Not applicable

21.Declaration (to be signed by all investigators)

By signing this form we give our consent to provide our expertise to the project. In addition:

a. We confirm that all investigators have approved this version of the protocol and have

contributed substantially to its development.

b. We confirm that all potential authors are included in this protocol.

c. We confirm that we shall submit any protocol amendments, significant deviations from

protocols, progress reports (if required) and a final report and also participate in any audit

of this study, if required.

Title of Research Project:

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d. We confirm that we shall conduct this study in accordance with the Declaration of

Helsinki; the ICMR Guidelines for Biomedical Research in Human Subjects 2006, with

any subsequent amendments; and all applicable laws of the land.

e. We also agree to submit for publication to a peer reviewed journal the complete results of

this study within two years of completion of this study.

f. We declare that we have no conflicts of interest that may affect the conduct or reporting

of this study (OR) we declare the following conflicts of interest below.

g. We are aware of the institution's policies regarding scientific misconduct

(Falsification/fabrication/plagiarism) and agree to abide by them.

22.Signature of Principal Investigator:

23.Signature of Guide/Head of the Department/ Unit:

24.Co-Investigator's Consent (all co-investigators have to sign this form or supply

separate letters of consent)

Name Department Signature Date

Dr. Munawwar Ahmed Radiology

Dr. Shyamkumar N Keshava Radiology

Dr. Vinu Moses Radiology

Dr. George Koshy Chiramel Radiology

Dr. C.E.Eapen Clinical Gastroenterology

and Hepatology

Dr. Uday George Zachariah Hepatology

Title of Research Project:

Institutional Review Board application form, Version 2.6, Sep 2015 Page 23

Dr. Ashish Goel Hepatology

Note: If the project is a resubmission a fresh copy of signatures needs to be obtained for

IRB submission.

Conflicts of interest if any:

SAMPLE INFORMATION SHEET & CONSENT FORM

Section III

CHECKLIST FOR PROTOCOLS SUBMITTED TO IRB OF CMC VELLORE FOR

OBSERVATIONAL

(CASE CONTROL, COHORT & CROSS SECTIONAL) STUDIES

Please tick the appropriate boxes below to indicate that the following have been submitted

and if not, please explain why:

1. Form for protocols of Observational Studies with all sections (I, and II) completed [√]

2. Informed consent sheet *and participant information sheet*in all relevant local languages

(PDF Format) [√]

3. Names, affiliations and signatures of all investigators/co-investigators for the declaration [√]

4. Signature of the Head of the department or unit as applicable (for interdepartmental

studies, an agreement letter from concerned departmental heads is desirable, especially if

they are not co-investigators). [√]

5. Recent curriculum vitae of all the investigators indicating qualification and experience and

relevant publications in the past five years. [√]

6. If applicable, proposed compensation and reimbursement of incidental expenses and

management of research related and unrelated injury/ illness during and after research

period. [Not applicable]

Title of Research Project:

7. If applicable (in study-related injuries), a description of the arrangements for insurance

coverage for research participants and copy of insurance documents from an India

insurance agency. [Not applicable]

8. If applicable; all significant previous decisions (e.g., those leading to a negative decision or

modified [Not applicable]

protocol) by other ECs or regulatory authorities for the proposed study and an indication of

the modification(s) to the protocol made on that account. The reasons for negative

decisions should be provided. [Not applicable]

9. Plans for publication of results - positive or negative - while maintaining the privacy and

confidentiality of the study participants, with names of proposed authors and their expected

contributions. [√]

10. All other relevant documents related to the study protocol like product information and

statement of relevant regulatory clearances. [√]

11. If applicable, any material used for advertisement to recruit participants to the study - this

may include flyers, brochures, posters, radio and TV advertisements. [Not applicable]

12. For externally funded studies, details of Funding agency/ Sponsors and breakdown of fund

allocation. [Not applicable]

13. One hard copy and a soft copy on CD to research@cmcvellore.ac.in of all the above.

[√]

Please list below all additional documents that are being submitted along with this

application including all appendices.

1. CV of guide and coinvestigator: Dr. Munawwar Ahmed

2. CV of coinvestigator: Dr. Shyamkumar N. Keshava

3. CV of coinvestigator: Dr. Vinu Moses

4. CV of coinvestigator: Dr. George Koshy Chiramel

5. CV of coinvestigator: Dr. C.E.Eapen

6. CV of coinvestigator: Dr. Uday George Zachariah

7. CV of coinvestigator: Dr. Asish Goel

8. CV of principal investigator: Dr. Manisha Mane

9. Information sheet and consent form in English

10.Information sheet and consent form in Hindi

11.Information sheet and consent form in Tamil

12.Information sheet and consent form in Bengali

13.Data collection sheet (Proforma)

14.Colour Doppler : TIPS stent format

Title of Research Project:

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Format for Informed Consent Form for Subjects

Informed Consent form to participate in a research study

Study Title:

Study Number: _____

Subject's Initials: _____ Subject's Name:

_____

Title of Research Project:

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I amfree to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that ***the Sponsor of the clinical trial, others working on the Sponsor's behalf (delete as appropriate)***, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).[ ]

(v) I agree to take part in the above study.[ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____Signature:

Or

Representative: _____

Title of Research Project:

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

Notes for filling in this form

1. Section I is required for Research Committee Approval and application for Fluid

Grants. Section II is required for Ethics Committee Approval. Section III contains a

checklist that should be filled and accompany this submission. (Incomplete

submissions will be rejected).

2. Please also read the **Standard Operating Procedure** of the IRB of CMC Vellore (available

from the Research website) for additional guidance on policies and procedures that will be

followed at CMC for IRB approval. Website link:

http://172.16.11.136/Research/IRB_Polices.html.

3. This form conforms to the requirements of the STROBE statement. An Explanation and

elaboration article discusses each checklist item and gives methodological background and

published examples of transparent reporting. The STROBE checklist is best used in

conjunction with this article (freely available on the Web sites of PLoS Medicine at

http://www.plosmedicine.org/ Annals of Internal Medicine at http://www.annals.org/and

Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available

at http://www.strobe-statement.org.

Research website link: http://172.16.11.136/Research/Flow%20chart.html.

Title of Research Project:

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4. Externally funded projects should also be submitted using this form, in addition to documentation provided by sponsors.

5. Submission procedure

Σ Project proposal,

Σ Curriculum Vitae's

Σ Information sheet and informed consent forms

Σ The aforesaid in translated versions need to be in **PDF format**.

Σ **Signatures by all investigators and the Guide/Head of the Department/Unit need to be scanned.**

Applications submitted after the due date will not be entertained.

6. It is mandatory to fill in the checklist (Section III)

Completed application with all supporting documents (Hard and Soft copy) should be submitted to:

Institutional Review Board,

ChristianMedicalCollege

Office of Research, I st Floor, Carman Block, Bagayam, Vellore 632 002 India.

E-mail: research@cmcvellore.ac.in.

Tel: 0416 -2284294, 2284202 Fax: 0416 – 2262788, 2284481.

Hours for submission: 8.00 am to 5.00 pm (Monday – Friday)

8.00 am to 12.00 pm (Saturday)

slno	age	sex	tipsdate	tipsindi	porthyp	hyperca	stenttyp	numofs	length1	diamete	stent2	length2	diamter	folluptil	batime	sympt	doppler	portal	midster	cavalen	mainpo	venogra	balloon	newste	stentty
1	59	2	19/07/2005	3	3		1	1	6	10				0		1	1								
2	45	1	27/02/2006	1	1		1	2	10	10		8	10	8	3 years	1	1						2	2	
3	28	2	19/08/2006	1	1		1	1	10	10		8	10	3	3-4 months	1	1								
4	25	2	26/02/2007	1	1		1	1						0		1	1								
5	35	2	18/04/2008	1	1		1	1	10	10				6	1 year	1	1								
6	18	1	20/04/2009	1	7		1	1	9	10				4		1	1		230	150					
7	42	2	27/09/2009	1	1		1	1				10	10	15		1	1						2	2	
8	45	1	26/08/2009	1	5		1	1	6	10				3	3-4 months	1	1								
9	22	1	26/08/2009	1	1		1	2	8	10	Fluency	4	10	8		1	1								
10	50	1	16/12/2009	1	2		1	1	10	10				1		1	1								
11	35	2	03/02/2010	1	1		1	2	10	10	Niti-S	9	10	12		1	1								
12	52	2	25/08/2011	1	1		1	1	8	10				1		1	1	207	163	203			2	2	
13	76	1	16/08/2012	1	5		1	1	4	10				0		1	1	198	202	180	10		2	2	
14	53	2	28/07/2010	1	1	2	1	1	8	10				7		1	1		80		30		2	2	
15	62	1	05/07/2010	1	4		1	1	8	10				0		1	1	100		70					
16	48	2	18/10/2010	1	1	1	1	2	10	10	fluency	4	10	9		1	1	120	130	100	30		2	1	
17	35	1	17/12/2010	1	1	2	1	2	10	10	fluency	4	12	7		1	1								
18	64	1	01/08/2011	1	1	2	1	1	8	10				0		1	1								
19	48	1	13/12/2011	3	2	2	1	1	8	10				11		1	1	108	149	152	84		2	2	
20	41	1	26/12/2011	1	1	2	1	1	10	10				11		1	1						2	2	
21	24	2	21/12/2011	1	1	1	1	1	10	10				6	1 year	1	1	110	120	200	70		2	1	
22	32	2	07/12/2011	1	1	2	1	1	10	10				0		1	1								
23														0		1	1								
24	32	2	31/08/2011	1	1	2	1	1						0											
25	51	2	05/09/2011	3	5	2	1	1	8	10				6		1	1								
26	35	2	21/10/2011	1	1	2	1	1	10	10				8		1	1								
27	20	1	07/03/2012	1	1	2	1	1	9	10				7	2 years	1	1								
28	52	2	14/03/2012	3	4	2	1	1	4	10				7		1	1						2	2	
29	15	1	30/04/2012	1	1	1	1	1	9	10				7	2 years	1	1						2	2	
30	34	2	30/07/2012	1	1	2	1	1	8	10				1		1	1								
31	34	1	16/07/2012	3	1	2	1	1	7	10				8		1	1								
32	45	1	20/08/2012	1	1	2	1	1	10	10				0		1	1								
33	22	1	14/09/2012	1	1	1	1	1	10	10				9		1	1						2	2	
34	32	2	21/03/2012	1	1		1	1	10	10				10		1	1								
35	28	1	10/07/2013	1	1		1	1	10	10				8		1	1						2	2	
36	62	1	03/08/2013	4	8	1	1	1	9	10				1		1	1						2	2	
37	54	1	21/08/2013	3	6	2	1	1	10	10				10		1	1								
38	21	1	13/09/2013	1	1	2	1	1	8	10				8		1	1								
39	47	1	25/09/2013	1	1	2	1	1	5	10				7		1	1						2	2	
40	19	1	16/10/2013	1	1	2	1	1	10	10				0		1	1								
41	16	2	30/10/2013	1	1	2	1	1	10	10				0		1	1								
42	25	1	08/01/2014	3	1	1	1	1	4	10				0		1	1								
43	13	2	01/02/2014	1	1	2	1	1	8	10				7	1nd 1/2 y	1	1								
44	29	2	17/02/2014	1	1	2	1	1	4	10				6		1	1								
45	32	1	19/02/2014	1	1	2	1	1	5	10				8		1	1								
46	35	1	24/02/2014	2	2	2	1	1	4	10				0		1	1								
47	37	1	30/05/2014	1	1	2	2	1	9	10				6		1	1								
48	58	1	15/09/2014	4	2	1	2	1	7	10				0		1	1								
49	23	2	29/12/2014	1	1	2	2	1	10	10				8		1	1								
50	54	1	06/03/2015	1	2	2	2	1	9	10				0	1 week	2	2					3	1	2	
51	41	1	11/03/2015	3	1	1	2	1	12	10				0	1 week	2	2					3	1		
52	20	1	11/05/2015	1	1	2	2	1	10	10				3		1	1								
53	65	1	27/05/2015	3	2	2	2	1	10	10				7		1	1								
54	47	2		2	1	2	2	1	10	10				7		1	1						2	2	
55	28	1	13/07/2015	1	1	2	2	1						6	1 year	1	1								
56	19	1	15/07/2015	1	1	2	2	1	10	10				0	1 week	2	2					3	1	2	
57	43	1	27/07/2015	1	1	2	2	1	12	10				0	1 week	2	1					2	1	2	
58	40	1	21/09/2015	1	2	2	2	1	10	10				0	1 week	2	2					3	1	1	Niti-S
59	41	1	05/10/2015	1	2	2	2	1	8	10				0		1	1								
60	55	1	26/10/2015	1	5	2	2	1	7	10				0		1	1						2	2	
61	24	1	11/11/2015	1	1									0		1	1								
62	24	1	11/11/2015	1	1	2	2	1	10	10				0		1	1								
63	56	1	21/11/2015	3	3	2	2	1	7	10				1		1	1								
64	49	1	25/01/2016	1	5	2	2	1	10	10				6		1	1	54	50	20	45		2	2	
65	57	1	22/01/2016	1	3	2	2	1	9	10				1		1	1	73	104	104	54		2	2	
66	25	1	28/01/2016	3	1	1	2	1	11	10				6	1 year	1	1	250	256	20	90		2	2	
67	43	2	04/04/2016	1	1	2	2	1	10	10				7		1	1								
68	56	1		4	4	2	2	1	9	10				3		1	1	89	239	135	45		2	2	
69	40	2	23/05/2016	1	1	2	2	1	11	10				0		1	1								
70	18	1	11/05/2016	1	1	2	2	1	12	10				6		1	1								
71	42	2	17/08/2016	1	1	2	2	1	12	10				0		1	1								
72	45	2	03/10/2016	1	2	2	2	1	6	10				6		1	1								
73	15	1	28/11/2016	1	1	2	2	1	9	10				4	6-7 month	1	1								
74	40	1	12/01/2017	1	1	2	2	1	11	10				4	6-7 months	1	1								
75	24	2	18/01/2017	1	1	2	2	1	11	10				4		1	1								
76	29	1	03/02/2017	1	1	2	2	1	10	10				4		1	1								
77	28	2	10/03/2017	1	1	2	2	1	11	10				4		1	1								
78	19	1	06/03/2017	3	1	2	2	1	10	10				4		1	1								
79	31	1	24/04/2017	1	1	2	2	1	12	10				4		1	1	154	148	146	132		2	2	
80	40	1	08/05/2017	1	2	2	2	1	8	10				1		1	1								
81	56	1	03/05/2017	1	3	2	2	1	10	10				1		1	1								
82	36	1	14/06/2017	1	1	2	2	1	8	10				0		1	1								
83	40	1	19/06/2017	1	1	2	2	1	9	10				1		1	1								

lenth2	diamter	email	sympt2	doppler	portal2	midster	cavalen	mainpo	venogra	balloon	newster	sympt4	doppler	portal4	midster	cavalen	mainpo	venogra	balloon	newster	telepho	sympt7	doppler	portal7	midster	cavalen	mainpo
			1	1								1	1									1	1				
			1	1								2	2			161		3	1	2							
			1	1								1	1	133	157	201	75					1	1				
			1	1								1	1									2	1				
			1	1		140	166					1	1									1	1				
			1	1								2	3		111	30		2	1	2							
			1	1								1	1	112	110	90	56		2	2		1	1				
			1	1	110	123	130			2	2																
			1	1								1	1									1	1	142	90	144	
			1	1	142		100			2	2																
			1	1								1	1									1	1				
			1	1								1	1									1	1	184	135	150	30
			1	1								1	1									1	1				
			1	1								1	1		100		20		2	2		1	1				
			1	1								1	1									1	1	96	121	120	
			1	1								1	1									2	1	219	145	142	
			1	1								1	1	197	97	98	50		2	2		1	1				
			1	1								1	1									1	1				
			1	1								1	1	59	79	108			2	2		1	1				
			1	1								1	1									1	1				
			1	1								1	1									1	1	130	120	110	
			1	1					1	2	2											1					
			1	1								1	1									1	1	255	246	151	
			1	1								1	1	80	107	114			2	2		1	1				
			1	1								1	1									1	1				
			1	1								1	1									1	1				
			1	1	106	99	65			2	2																
			1	1	108	96	107	48		2	2	1	1									1	1				
			1	1								1	1									1	1				
			1	1								1	1	105	106	81	34		2	1		1	1				
			1	1								1	1									1	1				
			1	1								1	1									1	1	95	119	127	54
			1	1								1	1									1	1	170	157	159	50
			1	1								1	1	204	143	203	54		2	2		1	1				
			1	1								1	1									1	1	114	100	91	54
			1	1								1	1	98	101	112	43		2	2							
			1	1								1	1									1	1	173	216	179	45
			1	1								1	1									1	1				
			1	1								1	1									1	1				
10	10																										
			1	1						1	1																
			1	1								1	1	94	100	112	75		2	1		1	1	78	90	100	34
			1	1	93	96	48	48																			
			1	1								1	1									1	1				
			1	1	110	142	122	40		2	2	1	1									1	1				
			1	1								1	1	125	270	175	45		2	2							
			1	1								1	1									1	1				
			1	1								1	1	178	116	168	60		2	1		1	1	123	178	123	40
			1	1								1	1									1	1	136	156	280	45
			1	1								1	1									2	2				
			1	1								1	1									1	1	98	100	90	45
			1	1								1	1									1	1	111	100	94	35
			1	1								1	1								asymto	1	1				
			1	1								1	1									1	1	112	94	98	34
			1	1								1	1	130	136	143	78		2	2		1	1	122	130	127	73
			1	1	200	210	210	50		2	2																
			1	1	153	220	236	77		2	2	1	1									1	1	223	215	230	72
		new syr	3	1																							

venogra	balloon	newster	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newster	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newster	telinf	sympt2	doppler	portal2	midster	cavalen
			1	1								1	1									3	1		100	
			1	2					3	1	1															
2	3	2																								
			1	1								1	1									1	1	112	120	112
			1	1								1	1									1	1			
	2	2	1	1	136	148	106	55		2	2	1	1									1	1	81	80	117
			1	1								1	1								no symt	1				
	2	2	1	1	184	160	150	30		2	2	1	1									1	1	165	179	157
			1	1	108	154	120			2	2	1	1									1	1	144	115	111
			1	1	120	90	100	24		2	2	1	1									1	1			
	2	2	1	1	110	143	115			2	2	1	1									1	1	139	149	104
4	2	2	2	3	220	160	140	24	2	1	2															
			1	1	151	136	99	51		2	2															
			1	1	119	102	116	32		2	2	1	1									1	1	91	184	144
			1	1	52	71	41			2	2	1	1									3	1	41	45	46
			1	1	131	120	141	54		2	2	1	1	157	132	150	50		2	2		1	1			
4	2	2	1	1	131	121	130			2	2	1	1									3	2			
1	2	2																								
	2	2	1	1	169	207	149			2	1	1	1									1	1	110	203	153
			1	1	80	110	114			2	2	1	1									1	1	140	128	118
			1	1	101	50	75	86		2	2	1	1									1	1			
			1	1								1	1									1	1	105	184	101
			1	1								1	1									1	1			
			1	1								1	1									1	1			
			1	1	105	106	81	37		2	1	1	1									1	1			
			1	1								3	3					2	1	2						
	3	2	1	1	155	114	91	36																		
	2	2	1	1	129	148	176	25		2	2	1	1									1	1	140	150	60
			1	3	172	276	166	163																		
	2	2	1	1																		1	1			
																						1	1	100	120	141
	2	2	1	1	172	172	144	40		2	2	1	1									1	1	86	90	92
			1	1	210	180	176	36		2	2	1	1									1	1	220	180	190
			2	2					2	1	2															
4	2	2	1	1						2	2															
			2	2					3	1	2															
			1	1								1	1									1	1	134	117	159
			1	1	90	100	120	53		2	2															
4	2	2	1	1	90	100	110	43		2	2															
2	1	2																								
3	1	2																								
	2	2																								
	2	2																								
	2	2																								
	2	2																								
	2	2																								

mainpo	venogra	balloon	newster	sympt3	doppler	portal3	midster	cavalen	mainpo	venogra	balloon	newster	sympt4	doppler	portal4	midster	cavalen	mainpo	venogra	balloon	newster	telinf1	sympt5	doppler	portal5	midster
	4	3	2	2	2					3	1	2														
	4	2	2	1	1								1	1	111	106	108	47					1	1		
				1	1	100	90	96	43		2	2														
55	4	2	2	1	1	75	96	109		4	2	2	1	1									1	1		
39		2	2										3	3					2	1	2					
78				1	1	114	115	111	78		2	2	1	1	193	155	151	52		2	2		1	1	152	117
				1	1						2	2	1	1									1	1		
32		2	2	1	1	110	143	115			1	1	1	1	90	130	120	23	1	2	2		1	1		
32		2	2	1	1	60	101	120	24		2	2														
	2	1	2																							
	3	1	2																							
																						no symtoms till 5 yrs no usg/dopler done				
		2	2	1	1	169	207	149			2	2														
40		2	2	1	1								1	1	42	87	81	16								
				1	1								1	1									1	1	97	111
46		2	2	1	1	108	100	85			2	2														
				1	1								1	1								outside	1	1		
				3	3	20	21	35	21	4	3															
		2	2																							
50		2	2	1	1	102	95	162	40		2	2														
				1	1	121	129	172	72																	
34	4	2	2																							
36		2	2																							
34	4	2	2																							
70		2	2																							

cavalen	mainpo	venogra	balloon	newster	sympt6	doppler	portal6	midster	cavalen	mainpo	venogra	balloon	newster	sympt7	doppler	portal7	midster	cavalen	mainpo	venogra	balloon	newster	sympt1	doppler	portal1
					1	1								1	1								1	1	78
														1	1	77	87	76	47	4	2	2			
					1	1	109	93	99			2	2	1	1	93	95	99	46	4	2	2			
104	11		2	2	1	1	115	146	114	41		2	2												
					1	1	70	100	112	42	1	2	2												
			2	2	1	1					4	2	2												
108	46		2	2																					
			2	2																					

midster	cavalen	mainpo	venogra	balloon	newste	ballangi	sympto	doppler	portalba	midster	cavalen	mainpo	venogra	balloon	lostfollo	followti	other	death	deathcause
						1													
89	97	27	4	2	2														
															1	0		1	death in 2014, exact cause not kown, documents NA.
															1			1	Phonic information, death in 2014,cause uncertain, documents NA
															1				
															1	0			
															1	0			
																3			
																		1	death on day 4 post TIPS, Liver ischemia/infarction
																	liver transplat		
																0		1	gagrene bowel, operated, death on post op day 1
																		1	operted for intestinal obstruction, post op unstable- death
																		1	on day 3 post TIPS, spontaeous bcterial peritoitis, AKI
																	liver trasplant 3		
																		1	day 2 post TIPS, hypotension during TIPS, worsened

slno	age	sex	ballangi	noba	batime	ballfup	sympt	doppler	portal	midster	cavalen	mainpo	venogra	balloon	newste	sympt2	doppler	portal2	midster	cavalen	mainpo
1	45	1	1	2	post 1st BA thrombosed at 6 monnths, 2nd BA not done	5										1	1				
2	28	2	1	3	6 months	11	1	1								3	2				
3	34	2	1	3	1 year, 2 year and 3 year	7	1	1						2	2	1	1				
4	45	1	1	1	5 month	5	1	1								1	1	141	119	201	45
5	20	1	1	2	1st at 3 years, 2nd at 5th years(2 years after 1st BA	7	1	1													
6	15	1	1	1	1 and half year	1	1	1													
7	24	2	1	3	1st at 3y,2nd at 1yr(postBA),3rd at 2 yrs(post 2 BA)	10	1	1								1	1				
8	13	2	1	3	1st at 1 and half year,2nd 2 mont(postb), 3rd 1y postba	7	1	1								3	3				
9	54	1	1	1	15th day	1	1	1													
10	54	1	1	1	1st week	7	1	1								1	1				
11	30	1	1	6	1 year	5	1	1								1	1				
12	19	2	1	1	1st week	5	1	1						2	2	1	1				
13	43	1	1	1	1st week	4	1	1								1	1				
14	25	1	1	1	1 year	1	1	1													
15	15	1	1	1	1 year	1	1	1													
16	10	1	1	1	1 year	1	1	1	123	135	131	28		2	2						

venogra	balloon	newste	sympt4	doppler	portal4	midster	cavalen	mainpo	venogra	balloon	newste	sympt7	doppler	portal7	midster	cavalen	mainpo	venogra	balloon	newste	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon
			1	1								3	2					4	3	2								
3	1	2																										
			1	1								1	1								3	3	130	125	200	18	2	1
	2	2	1	1					1	2	2	1	1								1	1					1	2
			1	1						2	2	1	1	41	42	36	23		2	2	1	1	31	56	136	12		2
			1	1								1	1								1	3	120	160	220	34	3	1
2	1	2																										
			1	1						2	2	1	1	56	100	50	26		2	2	1	3	65	46	297	17	2	3
			1	1								1	3						3	2	2	3	70	212	117	60	2	1
	2	2	1	1								1	1								3	3						3
			1	1								1	1	93	137	135	47		2	2								

newste	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newste	sympt2	doppler	portal2	midster	cavalen	mainpo	venogra	balloon	newste	lostfollo	followti	death	deathca	telphone	sympt3	doppler
2																									
2																									
2										1	1	46	45	41	30		2	2						3	3
																							asymtomatic, Dopper normal		
2																									
2	1	1								1	1	42	65	297	15		2	2							
2																									

portal3	midster	cavalen	mainpo	venogra	balloon	newste	sympt5	doppler	portal5	midster	cavalen	mainpo	venogra	balloon	newste	lostfollo	followti	death1	deathca	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newste
																		2		1	1							
				2	1																							

lostfollo	followti	ballang	symptb	doppler	portalba	midster	cavalen	mainpo	venogra	balloon	ballfup1	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newste	sympt2	doppler	portal2	midster	cavalen	mainpo	venogra	balloon
				2																								
		1	1	1						2		1	1	69	79	100	62		2	2	1	1	109	173	100	36		2
		1										1	1								1	1						
		1	1	1								1	1								1	1						
		1	1	1								1	1								1	1						
		1	1	1								1	1								1	1						
		1										1	1								2	3	46	259	94	29	2	1
		1										1	1															

newste	sympt4	doppler	portal4	midster	cavalen	mainpo	venogra	balloon	newste	sympt7	doppler	portal7	midster	cavalen	mainpo	venogra	balloon	newste	sympt1	doppler	lostfolu	portal1	midster	cavalen	mainpo	venogra	balloon	newste
2	3	3	28	30	24			1	2																			
										1	1								3	3		202	181	180	22	2	1	1
	1	1								1	1								1	1								
	1	1								1	1								3	3		160	130	360	35	2	1	2
	1	1								1	1								3	3						2	1	2
2																												
																			3	2	1							

stenttyp	length	diamete	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newste	sympt2	doppler	portal2	midster	cavalen	mainpo	venogra	balloon	newste	lostfoll	followti	death2	deathca	ballangi	symptb	doppler	portalba
																									1			
Viator C	10	10																							1	1	1	134
			1	1								2	3	60	70	180	20	2	1	2								
			1	1								2	3	200	360	180	27	2	1	2					1			
																									1	1	1	
																									1			

mainpo	venogra	balloon	newste	sympt7	doppler	portal7	midster	cavalen	mainpo	venogra	balloon	newste	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newste	sympt1	doppler	portal1	midster	cavalen	mainpo	venogra	balloon	newste	sympt2
				1	1	141	100	90	43		2	2																			
				1	1	119	159	220			2	2																			
53	2	1	2																											